(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 0 702 082 A1

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
20.03.1996 Bulletin 1996/12

(51) Int. Cl.[6]: **C12N 15/13**, C07K 16/42

(21) Application number: **94115683.8**

(22) Date of filing: **05.10.1994**

(84) Designated Contracting States:
AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

(30) Priority: **06.10.1993 JP 272950/93**

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(54) Amino acid sequences of anti-idiotypic antibodies against anti-cancer human monoclonal antibody, and dna base sequences encoding those sequences

(57) Amino acid sequences of the H chain and L chain variable regions of mouse monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 against idiotypes of a cancer cell antigen-specific human immunoglobulin CLN/IgG produced by a human/human fused cell strain CLN/SUZ H11, and base sequences of the genes of the variable regions are disclosed.

The above amino acid sequences and the base sequences are useful in medical and pharmaceutical fields such as prophylaxis, treatment and/or diagnosis of human diseases, and/or in pharmacological and/or biochemical fields, etc. such as biochemical reagents, and reagents for purification of biomacromolecules.

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Description

Detailed Description of the Invention

This invention relates to the structure of the variable regions of mouse immunoglobulins against idiotypes of an antigen-specific human immunoglobulin, useful in wide fields, for example in pharmaceutical fields such as prophylaxis, treatment and/or diagnosis of human diseases, and/or in pharmacological and/or biochemical fields such as biochemical reagents and reagents for purification of biomacromolecules.

More detailedly, this invention relates to the amino acid sequences of the H chain and L chain variable regions of mouse immunoglobulins against idiotypes of a cancer cell antigen-specific human immunoglobulin produced by a human/human fused cell strain CLN/SUZ H11 from a B cell of a patient carrying human cervical carcinoma and a human lymphoblastoid cell strain, and relates to the base sequences of the genes of the variable regions.

Since the development of the technique of formation of monoclonal antibodies by cell fusion or immortalization of cells, many useful antibodies have been obtained using mainly mice. Among them, monoclonal antibodies against malignant tumor cells are utilized not only for fundamental researches such as analyses of tumor antigens, but in serum diagnoses, image diagnoses of tumors using labeled antibodies, and have extremely high utilization value. Particularly, human-derived anti-cancer monoclonal antibodies are expected as ideal antibodies in the clinical field, since they have only faint or no side effects.

In such circumstances, one of the present inventors, as disclosed detailedly in Japanese Laid-Open Patent Publication No. 201994/1983 (= U. S. Patent No. 5,286,647; EP-A-839,02157.3), Japanese Laid-Open Patent Publication No. 135898/1984 and Japanese Laid-Open Patent Publication No. 137497/1984, established a cell strain CLN/SUS H11 (ATCC No. HB 8307) which produces a human monoclonal antibody having a high reactivity with human cancer cells. Interesting findings are obtained about the antibody (named CLN-IgG) produced by this cell strain, that the antibody class is IgG; the isotypes are γ1 type and κ type; and the antibody binds to a cancer antigen immunohistologically existing on the surface of the cancer cells and moreover inhibits proliferation of the cancer cells. At present, the whole amino acid sequence and DNA base sequence of the antibody are clarified (Japanese Laid-Open Patent Publication No. 346792/1992 = WO 92/20799).

On the other hand, since Jerne put forward the so-called network theory, various researches have been made on the structure of the variable regions of antibodies. An antibody binds to an antigen at its variable region (antigen combining site). Therefore, the variable regions of antibodies have various three-dimensional-like structures in accordance with the structures of the antigenic determinants on the surfaces of antigens to be recognized. Thus, an antibody itself can be considered to be an antigen, and in the case, the structures of the variable regions of the antibody are called idiotypes, and antibodies against the idiotypes of the antibody are called anti-idiotypic antibodies. The structure corresponding to an antigenic determinant is called an idiotope. An idiotype can be thought to be an aggregate of idiotypes. It was reported that among anti-idiotypic antibodies (Ab2) against an antibody (Ab1) exist antibodies which competitively inhibit binding of Ab1 to an antigen and have idiotopes analogous to antigens recognized by the antibodies, i.e. antibodies having structures as so-called internal images of the antigen.

In view of the above findings, anti-idiotypic antibodies are expected to be utilized for the purpose of treatment and/or diagnosis of cancers.

For example, as for the purpose of cancer treatment, a vaccine therapy using an anti-idiotypic antibody as an antigen is made possible. It is generally difficult to get cancer antigens in large amounts, and it is restricted from a safety aspect and an ethical aspect to directly immunize human beings with cancer cells as antigens. Therefore, these problems can be avoided by performing immunization with an anti-idiotypic antibody in place of an antigen.

In a diagnostic aspect, anti-idiotypic antibodies can be utilized to examine the state of immune reactions against cancer cells. Specifically, it serves for early detection of cancers, judgment of therapeutic effects to detect or determine one's antibodies against cancer antigens existing in the blood or humor of cancer patients.

Under such technical background, problems as stated below are underlying to be solved.

1) When anti-idiotypic antibodies are utilized as vaccines or diagnostic drugs, it is necessary to provide these antibodies in large amounts and stably. 2) There is a possibility to give more powerful vaccines or diagnostic drugs abounding in functionality by altering or modifying the antibodies.

A method by gene manipulation is considered as a means for solving the above problems, i.e. a means for realizing improvement of production amount of the antibodies and elevation or modification of the activities of the antibodies.

For example, in the case of the problem of 1), it can be considered to solve the problem by cloning such an antibody gene, introducing the gene into host cells such as animal cells or Escherichia coli, expressing the antibody gene to give a large amount of the antibody, and in the case of the problem of 2), it can be considered to alter such an antibody so as to have stronger immunogenicity by artificially changing the antibody gene, or to design an antibody molecule having a higher vaccinal activity by adding a function which the antibody does not inherently have, for example an enzymatic activity, an immunity induction activity or the like to the antibody molecule or a fragment thereof.

For accomplishment of these purposes, separation of anti-idiotypic antibody genes, and clarification of their structures are necessary. However, there has not so far been known anything at all about the structures of L chains and H chains constituting anti-idiotypic antibodies against idiotypes of CLN-IgG, and the gene structures of the variable regions having a function to specifically bind to idiotopes of CLN-IgG.

Thus the main object of this invention is to clarify the gene structures of the L chains and the H chains of anti-CLN-IgG idiotype antibodies.

The present inventors have succeeded in creating hybridomas producing, respectively, five kinds of mouse anti-CLN-IgG idiotype antibodies (Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33) having γ1 and κ isotypes against the idiotypes of CLN-IgG; have separated, from the hybridomas, cDNAs encoding the L chains and H chains of the anti-idiotypic antibodies, respectively; have clarified their DNA base sequences; have determined, based on these sequences, th amino acid sequences of the L chains and H chains of the antibodies, respectively; and have completed this invention.

Thus, according to this invention are provided an immunoglobulin H chain variable region fragment which contains a hypervariable region CDR1 having an amino acid sequence selected from

(1) Ser Tyr Trp Met His;
Asp Tyr Tyr Met Asn; and
Asn Tyr Trp Met Gln,

a hypervariable region CDR2 having an amino acid sequence selected from

(2) Ala Ile Tyr Pro Gly Asn Ser
Asp Ile Ser Tyr Ser Gln Asn
Phe Lys Asp;
Phe Ile Arg Asn Lys Ala
Asn Leu Tyr Thr Thr Asp
Tyr Ser Ala Ser Val Lys
Gly;
Phe Ile Arg Asn Lys Ala
Asn Tyr Tyr Thr Thr Glu
Tyr Ser Ala Ser Val Lys
Gly; and
Ala Ile Tyr Pro Gly Asp
Gly Asp Thr Arg Tyr Thr
Glu Lys Phe Lys Gly,

and a hypervariable region CDR3 having an amino acid sequence selected from

(3) Glu Glu Tyr Asp Tyr Asp
Thr Leu Asp Tyr;
Asp Arg Gly Gly Arg Asp
Trp Tyr Phe Asp Val;
Asp Gly Phe Leu Arg Asp
Trp Tyr Phe Asp Val; and
Ser Gly Tyr Tyr Gly Ser
Phe Val Gly Phe Ala Tyr ;

and DNA and RNA fragments encoding the immunoglobulin H chain variable region fragment.

According to this invention are further provided an immunoglobulin L chain fragment which contains a hypervariable region CDR1 having an amino acid sequence selected from

(1) Tyr Arg Ala Ser Lys Ser Val
Gln Leu His Leu Ala Ile Val
Tyr Met His;
Tyr Arg Ala Ser Lys Ser Val
Ser Thr Ser Gly Tyr Ser Tyr
Met His;
Lys Ala Ser Gln Asp Val Asn
Thr Ala Val Ala; and
Lys Ala Ser Gln Asp Val Thr
Thr Asp Val Ala ,

a hypervariable region CDR2 having an amino acid sequence selected from

(2) Leu Val Ser Asn Leu Glu Ser;
Leu Val Ser Asn Leu Asp Ser; and
Ser Ala Ser Tyr Arg Tyr Thr,

and a hypervariable region CDR3 having an amino acid sequence selected from

(3) Gln His Ile Arg Val Ala Tyr Thr;
Gln His Ile Arg Gly Ala Tyr Thr;
Gln His Ile Glu Gly Ala Tyr Thr;
Gln Gln His Tyr Ser Pro Pro Leu Thr; and
Gln Gln His Tyr Ser Thr Ala Trp Thr;

and DNA and RNA fragments encoding the immunoglobulin L chain variable region fragment.

In this invention, cytoplasmic RNAs were prepared from the five mouse hybridomas, respectively; the RNAs were converted to cDNAs by a reverse transcriptase; the antibody genes were amplified using these cDNAs as templates and using the PCR method; the amplified DNA fragments were integrated into plasmids and cloned; the base sequences of the insertion DNAs of the plasmids purified from Escherichia coli clones isolated were determined, and the amino acid sequences were determined based on the base sequences. These steps are further detailedly described below.

[1] Isolation of cytoplasmic RNAs

Each mouse hybridoma is cultured and proliferated in a culture medium, e.g. and RDF or RPMI 1640 medium, containing 5% fetal bovine serum under a suitable condition, e.g. under a condition of 37°C and a carbon dioxide concentration of 5%; the resultant cells are collected by centrifugation; and the cytoplasmic RNA is extracted from the cells by a conventional method, e.g. a method disclosed in 7.12 of Molecular Cloning (2nd edition, edited by Sambrook et al., Cold Spring Harbor Laboratory Press 1989). The resultant cytoplasmic RNA can further be utilized as a template for cDNA synthesis. Specifically in this invention, the cytoplasmic RNAs were extracted from mouse hybridomas No. 3, No. 17, No. 20, No. 27 and No. 33, and provided for synthesis of cDNAs.

[2] Synthesis of cDNAs

Using a cytoplasmic RNA obtained in the step of [1] as a template, a single-strand DNA complementary to the mRNA is synthesized in the presence of dATP, dGTP, dTTP and dCTP using, as a primer, an oligo dT corresponding to a poly A, or a synthetic nucleotide having a random sequence, and a reverse transcriptase. In the specific operations in the invention, cDNAs were synthesized using the cytoplasmic RNAs obtained in the step of [1] as templates and a random hexamer as a primer, respectively, and provided for the step of amplification of the antibody genes.

[3] Amplification of antibody genes by PCR

PCR reaction is performed in the presence of dATP, dGTR, dTTP, dCTP and Taq polymerase using as a template a single-strand cDNA obtained in the step of [2] and as a primer a sequence of the antibody gene (e.g., a sequence encoding a constant region, a variable region or a leader region of the antibody gene) to amplify the antibody gene. Suitably in the invention, the antibody genes were amplified using as templates the single-strand cDNAs obtained in the step of [2] and using synthetic DNA oligomers corresponding to the sequences of the leader regions and variable regions of the L chains and H chains of the antibodies, respectively.

[4] Cloning of PCR-amplified DNA fragments

A PCR-amplified DNA fragment obtained in th step of [3] is, directly or after treatment with restriction enzyme(s), ligated into one of various vectors, for example plasmid vectors such as pUC 18, pCR1000 and pCR™ , phage vectors such as M 13 phage, and phagemid vectors such as pUC 118 and pBluescrpt SK* to prepare a vector containing the insertion fragment. Then, Escherichia coli is transformed with the vector, and a colony of the Escherichia coli containing

the targeted antibody gene fragment is obtained. The purified vector recovered from the Escherichia coli is provided as a sample for determination of the DNA base sequence. In the specific operations in the invention, the PCR-amplified DNA fragments obtained in the step of [3] were directly ligated, respectively, into pCR1000 and pCR™ plasmid vector; an Escherichia coli INVαF' was transformed with each of the resultant plasmids; and th plasmids were purified from the resultant Escherichia coli colonies, respectively.

[5] Determination of the base sequ nces and amino acid sequences of the DNAs

The base sequence of the DNA at the insertion site in a plasmid obtained in the step of [4] can be determined using the Maxam-Gilbert method or the Sanger method. In the invention, the pCR1000 or pCR™ plasmid vectors containing the insertion fragments were purified, respectively; their base sequences were determind by the Sanger method; and the amino acid sequences were presumed based on their base sequences, respectively.

Hereafter, this invention is further specifically described below according to examples.

Drawings referred to in Examples are briefly described as follows.

Fig. 1 is a drawing showing isotypes of monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33.

Fig. 2 is a drawing showing the monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 specifically bind to CLN-IgG, and do not bind to other human IgGs.

Fig. 3 is a drawing showing that monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 are competitively inhibiting the binding between CLN-IgG and human matrical carcinoma cell ME-180.

Fig. 4 is a drawing where the amino acid sequences of the H chain variable regions of monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 are notated in parallel according to the Kabat's notation, and the regions of the hypervariable regions CDR1, CDR2 and CDR3 are determined.

Fig. 5 is a drawing where the amino acid sequences of the L chain variable regions of monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 are notated in parallel according to the Kabat's notation, and the regions of the hypervariable regions CDR1, CDR2 and CDR3 are determined.

Example 1: Preparation of mouse hybridomas

100 µl of 1 mg/ml human IgG (produced by Cappel) is intraperitoneally injected to a Balb/c mouse on the first day after its birth to prepare a mouse having immunological tolerance to human IgG. Six weeks later, the mouse is immunized as follows with CLN-IgG as an antigen.

CLN-IgG purified from a culture medium of a human/human hybridoma CLN/SUZ H11 (ATCC No. HB8307) according to an ammonium sulfate precipitation method and protein A-affinity chromatography was adjusted to a concentration of 2 µg/µl with physiological saline; an equal amount of complete Freund's adjuvant solution was added; and after mixing and emulsification, 100 µl of the emulsion (corresponding to 100 µg of CLN-IgG) was subcutaneously injected into th immunologically tolerated mouse. Thereafter, similar immunization was repeated 4 to 5 times, the murine spleen was enucleated 4 days after the final immunization and made to be spleen cells, and they were used for the following cell fusion.

A mouse parent cells NS-1 (ATCC TIB 18) and the spleen cells are washed with portions of RPMI 1640 medium not containing serum, respectively, and the both of the cells are mixed and centrifuged. 1 ml of 50% polyethylene glycol (average molecular weight.: 4,000) is added dropwise to the resultant precipitate over a period of 1 minute. 10 ml of RPMI 1640 medium is further added over a period of 3 minutes, the mixture is centrifuged at 400 x g for 5 minutes, th precipitate is suspended in 10 ml of RPMI 1640 medium containing 20% fetal bovine serum, and the suspension is spread into a 96-well microplate.

Thereafter, the cells were cultured in HAT medium for 14 to 21 days, transferred to HT medium, and finally cultured in RPMI 1640 medium containing 10% fetal bovine serum.

The antibody titers in the culture supernatants on the wells where proliferation was observed were assayed by an enzyme-labeled antibody technique; hybridoma clones secreting monoclonal antibodies which bind to CLN-IgG but not to human IgG were obtained from the appropriate wells by the limiting dilution method; and these hybridoma clones were named No. 3, No. 17, No. 20, No. 27 and No. 33.

Example 2: Determination of isotypes of the mouse antibodies

Isotypes of the antibodies secreted from the 5 mouse hybridomas obtained in Example 1 were determined as follows using a mouse monoclonal antibody isotyping kit (produced by Amersham Co.).

The mouse hybridomas are started to be cultured at a concentration each of 5 x 10^4/ml in portions of RPMI 1640 medium containing 10% fetal bovine serum, respectively, and 5 days later the culture supernatants are obtained, one stick portions of the typing sticks are placed in test tubes, respectively; 3 ml portions of the culture supernatants 5-fold diluted with TBS-T (Tris-buffered saline (TBS, pH 7.6) containing 0.1% Tween 20) ar added thereto respectively; and

the mixtures are incubated at room temperature for 15 minutes. The culture supernatants are discarded, 5 ml portions of TBS-T are added, and the typing sticks are washed at room temperature for 5 minutes. TBS-T was discarded, and the washing was repeated once more. 3 ml portions of a p roxidase-labeled anti-mouse antibody 500-fold diluted with TBS-T are added, and the mixtures are incubated at room temperature for 15 minutes. The typing sticks are washed twice in the same manner as above; 3 ml portions of an enzyme substrate solution (obtained by adding ne drop of 30% aqueous hydrogen peroxide to 50 ml of a TBS solution of 4-chloro-1-naphtol) are added; the mixtures are subjected to reaction at room temperature for 15 minutes; and then the sticks are washed with distilled water. The isotypes of th mouse antibodies are determined based on the resultant signals, respectively.

As a result, as shown in Fig. 1, all the isotypes of these antibodies were $\gamma 1$ and κ.

Example 3: Examination of specificities of the anti-idiotypic antibodies

It was examined according to a dot blot technique, using an ECL Western blotting detecting reagent (produced by Amersham Co.), that the mouse anti-CLN-IgG idiotype antibodies specifically bind to CLN-IgG. The process is stated below.

CLN-IgG and human IgG1 (produced by Protogen Co.) were diluted with PBS to concentrations of 50 to 0.2 µl/ml, respectively. 2 µl portions of the thus prepared samples were spotted on a number of Hybond-ECL nitrocellulose membrane (produced by Amersham Co.), respectively and after being dried, the nitrocellulose membranes were allowed to stand at room temperature for one hour in PBS-T (0.3% Tween 20-containing PBS) containing 5% skim milk. After being washed with PBS-T, the nitrocellulose membranes were allowed to stand at room temperature for one hour in the culture supernatants (500-fold diluted with PBS-T) of mouse hybridomas No. 3, No. 17, No. 20, No. 27 and No. 33, respectively. After being washed with PBS-T, the nitrocellulose membranes were allowed to stand at room temperature for one hour in portions of a peroxidase-labeled sheep anti-mouse Ig antibody 3,000-fold diluted with PBS-T, respectively. After being washed with PBS-T, the nitrocellulose membranes were subjected to reaction for one minute in portions of the ECL detecting reagent, and sheets of X-ray film were exposed for 30 seconds to the light emitted from the resultant nitrocellulose membranes, respectively.

The results of the sheets of X-ray film developed are shown in Fig. 2. Any of the five antibodies bound to CLN-IgG, but did not bind to human IgG1. Namely, it was revealed that these antibodies are specific to CLN-IgG.

Next, it was examined whether or not the mouse antibodies have an activity to inhibit the binding of a human monoclonal antibody CLN-IgG to a human cancer cell. The method is stated below.

A human cervical carcinoma cell ME-180 (available from ATCC) is cultured in DF medium (a 1:1 mixed medium of DME : F-12) containing 10% fetal bovine serum. At the stage when the number of the cells becomes 5×10^6 to 1×10^7, the cells are detached from the bottom face of the Petri dish using trypsin, collected by centrifugation and sufficiently washed with the medium. A constant number (10^5/100 µl) each of the cells is placed in each well of a 96-well microtiter plate, and allowed to stand at 37°C overnight to be attached on the plate. 50 µl portions of 3% glutaraldehyde solution were added dropwise into the respective wells, and the mixtures are allowed to stand at 37°C for 20 minutes to fix the cells. The cells of each well are centrifuged at 200 x g for 10 minutes and washed three times with a gelatin buffer (10 mM phosphate-buffered physiological saline containing 0.3% gelatin); 200 µl portions of 1% bovine serum albumin (BSA) solution are added dropwise; and the mixture is allowed to stand at 37°C for one hour to block the plate. The cells are washed three times with the gelatin buffer to remove BSA not adsorbed. Thereafter, dilutions at various rates (100 to 1,000,000-fold) of the ascites obtained by intraperitoneally inoculating into mice the various hybridomas secreting the mouse anti-idiotypic antibodies are added dropwise together with CLN-IgG (50 µg each), and the mixtures are subjected to reaction at 37°C for one hour. The cells of these wells are washed three times with the gelatin buffer, 50 µl portions of a 3,000-fold diluted peroxidase-conjugated goat anti-human Ig antibody (produced by TACO Co.) are added dropwise, respectively, and the mixtures are subjected to reaction at 37°C for 30 minutes. The cells are washed three times with the gelatin buffer, and portions of a substrate solution containing hydrogen peroxide and o-phenylenediamine are added to perform reaction in a darkroom. 10 minutes later, 50 µl portions of 5N sulfuric acid are added to stop the reaction. When the peroxidase-conjugated goat anti-Ig antibody remains on the microplate, namely when the human IgG to be bound thereto remains, a yellow reaction product having absorption at 490 nm is formed. The amount of CLN-IgG bound to the cancer cell is determined by measuring the amount of the reaction product by a spectrometer.

It was clarified, according to the above method, that all the mouse antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 inhibit the binding of CLN-IgG to the cancer cell (Fig. 3).

From the foregoing, these mouse antibodies are antibodies against the idiotypes of CLN-IgG.

Example 4: Preparation of RNA

From the five kinds of mouse hybridomas No. 3, No. 17, No. 20, No. 27 and No. 33, the cytoplasmic RNAs were extracted according to the method disclosed in Molecular Cloning (2nd edition, edited by Sambrook et al., Cold Spring Harbor Laboratory Press 1989) 7, 12, as stated below.

10^8 each of the hybridomas cells are collected by centrifugation, and washed twice with 10 times each precipitate's volume of a phosphate-buffered saline. The cells of these groups are centrifuged at 2,000 x g and 4°C for 5 minutes, and the resultant precipitates are suspended in 200 µl portions of an RNA extracting solution (0.14 M NaCl, 1.5 mM $MgCl_2$, 10 mM Tris-HCl pH 8.6, 0.5% Nonidet P-40, 1 mM dithiothreitol, 20 mM vanadylribonucleoside complex), respectively. The suspensions are subjected to vortex for 15 seconds and allowed to stand on ice for 5 minutes. The resultant suspensions are centrifuged at 12,000 x g for 30 seconds to remove the cell nuclei as precipitates; to the supernatants are, respectively, added 200 µl portions of a proteinase buffer (0.2 M Tris-HCl pH 8.0, 25 mM EDTA pH 8.0, 0.3 M NaCl, 1.2% SDS) and 1 µl portions of an aqueous proteinase K solution (20 mg/ml); and the mixtures are sufficiently stirred and subjected to incubation at 37°C for 30 minutes. Equal volume portions of phenol/chloroform are added to the reaction solutions, respectively, and the mixtures are stirred, centrifuged at 5,000 x g and room temperature for 10 minutes, and then allowed to separate into organic layers and aqueous layers, respectively. 400 µl portions of isopropanol cooled on ice in advance are added to the aqueous layers recovered, respectively, and the mixtures are allowed to stand on ice for 30 minutes. The mixtures are centrifuged at 12,000 x g and 4°C for 10 minutes to collect RNAs. The resultant RNA precipitates are washed with 1 ml portions of ethanol, dried under reduced pressure and suspended in appropriate amount portions of TE buffer, respectively. Using the cytoplasmic RNAs obtained according to the above operations, the antibody genes are amplified.

Example 5: Amplification and cloning of the antibody genes by the RT-PCR method

The antibody genes were amplified from the cytoplasmic RNAs obtained in Example 4, using a GeneAmp® RNA PCR kit (produced by Takara Shuzo Co., Ltd.). First, 20 µl each of reactive solutions were prepared containing PCR buffer II (x1), 5 mM $MgCl_2$, 1 mM dATP, 1 mM dGTP, 1 mM dTTP and 1 mM dCTP, 1 U/µl an RNase inhibitor, 2.5 µM a random hexamer, 2.5 U/µl a reverse transcriptase and 100 ng each of the above-mentioned cytoplasmic RNAs, respectively; 20 µl portions of a mineral oil were overlaid thereon respectively; and incubations were performed at room temperature for 10 minutes, at 42°C for 15 minutes, at 99°C for 5 minutes and then at 4°C for 5 minutes to perform cDNA synthesis by reverse transcription reaction. Then, 80 µl portions of a solution consisting of 4 µl of 25 mM $MgCl_2$, 8 µl of 10x PCR buffer II, 65.5 µl of sterile distilled water, 0.5 µl of AmpliTaq DNA polymerase (5 U/µl) and 2 µl of PCR primers (each 100 pmoles) were added to the above 20 µl of the reverse transcription reaction solutions; 80 µl portions of the mineral oil were overlaid thereon; and PCR reactions were succeedingly performed. Each reaction was performed by repeating 30 times the cycle of 94°C for 1.5 minutes, 50°C for 2 minutes and then 72°C for 3 minutes. The base sequences of the PCR primers are shown below. The primers contained in a Ig-Prime™ kit (produced by Novagen Co.) were used except for the primer of the leader sequence C for H chains.

Primer for H chains	
Leader sequence A	5' GGGAATTCATGRASTTSKGGYTMARCTKGRTTT 3'
Leader sequence B	5' GGGAATTCATGRAATGSASCTGGGTYWTYCTCTT 3'
Leader sequence C	5' TTAAATGGTATCCAGTGT 3'
Constant region	5' CCCAAGCTTCCAGGGRCCARKGGATARACIGRTGG 3'

Primer for L chains	
Leader sequence A	5' GGGAATTCATGRAGWCACAKWCYCAGGTCTTT 3'
Leader sequence B	5' GGGAATTCATGGAGACAGACACACTCCTGCTAT 3'
Constant region	5' CCCAAGCTTACTGGATGGTGGGAAGATGGA 3'

In the above, the alphabets other than A, G, C and T mean the following bases. R=A/G, W=A/T, I=inosine, Y=C/T, D=A/G/T, K=G/T, H=A/C/T, S=C/G, V=A/C/G, M=A/C, B=G/C/T

10 µl portions of the resultant 100 µl each of the PCR reaction products are subjected to 1.5% agarose gel electrophoresis, and it was confirmed that the antibody gene fragments each about 600 bp long were amplified. As a result, in the case of the H chains, the antibody genes derived from No. 3 and No. 17 were amplified in the leader sequence A,

the antibody genes derived from No. 20 and No. 27 were amplified in the leader sequence B, and the antibody gene derived from No. 33 was amplified in the leader sequence C. On the other hand, in the L chains, the antibody genes derived from No. 27 and No. 33 were amplified in the case where the leader sequ nce A was used, and the antibody genes derived from No. 3, No. 17 and No. 20 were amplified in the leader sequence B.

Each of the PCR-amplified fragments about 600 bp long was integrated into pCR 1000 vector or pCR™ vector using TA cloning kit (produced by Invitogen Co.). Specifically, ligation mix solutions were prepared by mixing 1 µl portions of the PCR reaction products, 1 µl portions of 10 x the ligation buffer, 2 µl portions of pCR1000 or pCR™ vector (corresponding to 50 µg), 1 µl of T4 DNA ligase and 6 µl portions of sterilized water, respectively; and incubated overnight at 12°C. Separately, 50 µl portions of a suspension of a competent Escherichia coli INVαT' strain, to which portions were added 2 µl portions of 0.5 M β-mercaptoethanol, respectively, were prepared; and 1 µl portions of the above ligation mix solutions are added thereto, respectively. The mixtures are allowed to stand on ice for 30 minutes, incubated at 42°C for one minute, and rapidly cooled on ice for 2 minutes. 450 µl portions of SOC medium warmed to 42°C in advance were added to the resultant Escherichia coli solutions, respectively, and the mixtures are cultured with shaking at 37°C for one hour. Meanwhile, 25 µl portions of X-Gal (40 mg/µl) are spreaded onto a number of LB agar plates each containing Kanamycin (50 µg/ml), respectively, and the agar plates are incubated at 37°C until each X-Gal completely permeates the agar plate.

200 µl portions of the Escherichia coli culture broths after completion of culture were spread on the agar plate dried, respectively, and the plates were allowed to stand at 37°C overnight to give white colonies each having Kanamycin resistance.

Plasmids were purified from the Escherichia coli clones containing the respective antibody genes, and named 3KB11, 17KB1, 20KB1, 27KA2, 33KA26, 3GB1, 17GB7, 20GA2, 27GA5 and 33GC003, respectively. Purification of the plasmids is performed as follows.

The Escherichia coli strains containing the above plasmids, respectively, are cultured 37°C overnight in 100 ml portions of LB medium containing Kanamycin (50 µg/ml), respectively. Each of the resultant culture broths is centrifuged at 3,000 rpm for 10 minutes; the cells collected are suspended in 3 ml of an ice-cooled suspension (50 mM glucose, 10 mM EDTA, 2 mM Tris-HCl pH 8.0); and the suspension is allowed to stand at room temperature for 5 minutes. 6 ml of an alkali lysing solution (0.2 N sodium hydroxide, 1% SDS) is added, and the mixture is mixed by gently turning the centrifugation vessel upside down, and allowed to stand on ice for 5 minutes. 4.5 ml of an ice-cooled neutralizing solution (5 M potassium acetate pH 4.8) is added, and the mixture is centrifuged at 12,000 rpm and 4°C for 10 minutes. The supernatant is transferred into another centrifugation vessel; 1 ml of heat-treated 100 µg/ml RNase A solution is added; and the mixture is subjected to reaction for one hour in an incubator of 37°C to perform RNA digestion. To the reaction solution are added 6 ml of TE buffer-saturated phenol and 6 ml of chloroform/isoamyl alcohol (24:1), and the mixture is subjected to vortex for 30 seconds and then centrifuged at 10,000 rpm and 4°C for 3 minutes. The aqueous layer is transferred into another centrifugation vessel, an equal amount of isopropanol is added, and the mixture is sufficiently mixed and then centrifuged at 10,000 rpm and room temperature for 10 minutes.

The resultant precipitate is washed with 1 ml of 70% cold (-20°C) ethanol, dried under reduced pressure, and dissolved in 480 µl of sterilized water. The solution is transferred into an Eppendorf tube; 120 µl of 4 M NaCl and 600 µl of 13% polyethylene glycol #6000 are added; and the mixture is allowed to stand on ice for 20 minutes. The mixture is then centrifuged at 10,000 rpm and 4°C for 10 minutes, and the precipitate is washed with 1 ml of 70% cold (-20°C) ethanol, dried under reduced pressure and dissolved in 100 µl of TE buffer. The resultant purified plasmid was used as a template for sequencing reaction.

Example 6: Determination of the base sequences

Sanger reactions were performed using as templates the plasmids cloning purified in Example 5 and a fluorescence-labeled primer; the reaction products were analyzed by a DNA sequencer DSQ-1 (produced by Shimadzu Corporation); and the DNA base sequences of the insert parts of the plasmids were also determined.

The sequencing reactions were performed using AmpliTaq cycle sequencing kit (produced by Takara Shuzo Co., Ltd.) and a fluorescence-labeled primer in a reagent kit (produced by Wakunaga Pharmaceutical Co., Ltd.) exclusively used for a fluorencene-type DNA sequencer. First, 2 to 4 µg of one of the plasmids purified as stated in Exampl 5 is mixed with 1 µl of the FITC-labeled primer (1 p mole/µl, forward or reverse is used) and 2 µl of the 10 x cycling mix solution, and sterilized water is added to prepare 10 µl in final volume of a reaction mix. Four tubes are prepared in which 2 µl portions of the termination mix (A, G, C, T) were placed in advance, respectively. 2 µl portions of the above reaction mix were taken and placed into the respective tubes. The mixtures are corrected by centrifugation, 10 µl portions of a mineral oil are overlaid, and cycling reactions are performed under the following conditions; Precycle 95°C, 3 minutes; first cycle 95°C 30 seconds, 60°C 30 seconds, 72°C 1 minute (repeated 15 times); second cycle 95°C 30 seconds, 72°C 1 minute (repeated 15 times); postcycle 4°C.

2 µl portions of a reaction-stopping dye solution (95% formaldehyde, 20 mM EDTA, 0.05% methyl violet) are added, and the mixtures are mixed by centrifugation and preserved at 20°C until they are electrophoresed.

As 5% polyacrylamide gel was used one obtained by adding pure water to 50 g of urea, 6 ml of 10 x TBE buffer (0.89 M Tris-HCl, 0.89 M boric acid, 0.025 M EDTA disodium salt) and 10 ml of 30% acrylamide solution (28.5% acrylamide and 1.5% methylenebisacrylamide, both produced by BIO-RAD Co.) to make the whole volume 60 ml; filtering the mixture with 0.22-μm filter; deaerating the filtrate for 30 minutes; adding 150 μl of 10% ammonium persulfate and 15 μl of TEMEO; allowing the mixture to stand overnight to make it gel.

The gel was set in the DNA sequencer DSQ-1, and prerun was performed at a constant voltage of 1,000 V for one hour. Each of the samples was denatured at 95°C for 3 minutes immediately before electrophoresis, and rapidly cooled on ice, and 2 to 3 μl of the reaction solution was sucked up from the bottom part of the tube by a micro-syringe and loaded onto the gel. Samples run was performed at a constant electric power of 20 W for 12 hours.

After completion of electrophoresis, the base sequence was determined using the software attached to DSQ-1. The sequence was confirmed by sequencing both of the sense and antisense chains of the same plasmid from both directions.

The resultant base sequences of the variable regions of the H chains and L chains of the five kinds of the mouse monoclonal antibodies, and amino acid sequences presumed therefrom are shown in the following sequence listing. Relation between the sequence numbers and the sequences of the clones are as follows:

Sequence No. 1 : Idio 3 H chain variable region (clone 3GB1)
Sequence No. 2 : Idio 17 H chain variable region (clone 17GB7)
Sequence No. 3 : Idio 20 H chain variable region (clone 20GA2)
Sequence No. 4 : Idio 27 H chain variable region (clone 27GA5)
Sequence No. 5 : Idio 33 H chain variable region (clone 33GC003)
Sequence No. 6 : Idio 3 L chain variable region (clone 3KB11)
Sequence No. 7 : Idio 17 L chain variable region (clone 17KB1)
Sequence No. 8 : Idio 20 L chain variable region (clone 20KB1)
Sequence No. 9 : Idio 27 L chain variable region (clone 27KA2)
Sequence No.10 : Idio 33 L chain variable region (clone 33KA26)

Example 7 Determination of hypervariable regions

The amino acid sequences obtained in Example 6 were notated in parallel according to the numbering of Kabat et al.'s data base (Sequences of proteins of immunological interest Fifth edition, U. S. Department of health and human services. Public health service, National Institutes of Health. NIH Publication No. 91-3242, Kabat et al. 1991), and the amino acid sequences of the hypervariable regions CDR1, CDR2 and CDR3 of each antibody were identified (Fig. 4, H chains, Fig. 5 L chains). In order to confirm the novelty of the identified amino acid sequences of the hypervariable regions CDR1, CDR2 and CDR3, retrieval by a computer was performed using the above Kabat et al.'s data base and a protein data base NBRF-PDB (National Biomedical Research Foundation - protein data base) Release 36.

As a result, the amino acid sequences of Idio 3 H chain CDR1, Idio 17 H chain CDR1, Idio 20 H chain CDR1, Idio 27 H chain CDR1, Idio 33 H chain CDR2, Idio 3 L chain CDR2, Idio 17 L chain CDR2, Idio 27 L chain CDR2 and Idio 33 L chain CDR2 were the same as those of known antibodies, but the amino acid sequences of other CDRs were

revealed to be novel sequences.

Sequence Listing

Seq. I.D. number : 1

Sequence length : 399

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..399

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..27

Characteristics determination method : S

Sequence

```
CTG TCG GTA ACT TCA GGG GTC TAC TCA GAG GTT CAG CTC CAG CAG TCT    48
Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln Gln Ser
                -5                  1                   5

GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC AAG    96
Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys Lys
        10                  15                  20

GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA CAG   144
Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys Gln
    25                  30                  35

AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA AAT   192
Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
40                  45                  50                  55

AGT GAT ATT AGC TAC AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG ACT   240
Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu Thr
                60                  65                  70

GCC GTC ACA TCC ACC AGC ACT GCC TAC ATG GAA CTC AGA AGC CTG ACA   288
Ala Val Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr
            75                  80                  85

AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT TAC   336
Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asp Tyr
        90                  95                  100

GAC ACC CTG GAC TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TCC TCA   384
Asp Thr Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
    105                 110                 115

GCC AAA ACG ACA CCC                                              399
Ala Lys Thr Thr Pro
120
```

Sequence Listing

Seq. I.D. number : 2

Sequence length : 402

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..402

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..30

Characteristics determination method : S

Sequence

```
ATT CTG TCG GTA ACT TCA GGG GTC TAC TCA GAG GTT CAG CTC CAG CAG    48
Ile Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln Gln
-10                 -5                   1                   5
TCT GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC    96
Ser Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys
                10                  15                  20
AAG GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA   144
Lys Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys
            25                  30                  35
CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA   192
Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly
        40                  45                  50
AAT AGT GAT ATT AGC TAC AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG   240
Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu
    55                  60                  65
ACT GCC GTC ACA TCC ACC AGC ACT GCC TAC ATG GAA CTC AGA AGC CTG   288
Thr Ala Val Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu
70                  75                  80                  85
ACA AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT   336
Thr Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asp
                90                  95                  100
TAC GAC ACC CTG GAC TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TCC   384
Tyr Asp Thr Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
            105                 110                 115
TCA GCC AAA ACG ACA CCC                                          402
Ser Ala Lys Thr Thr Pro
        120
```

Sequence Listing

Seq. I.D. number : 3

Sequence length : 438

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..438

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..57

Characteristics determination method : S

Sequence

```
ATG GAG TTC GGG CTA AAC TGG GTT TTC CTT GTA ACA CTT TTA AAT GGT    48
Met Glu Phe Gly Leu Asn Trp Val Phe Leu Val Thr Leu Leu Asn Gly
                -15                 -10                 -5

ATC CAG TGT GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG    96
Ile Gln Cys Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Gln
            1                   5                  10

CCT GGG GGT TCT CTC AGA CTC TCC TGT GCA ACT TCT GGG TTA ACC TTC   144
Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Leu Thr Phe
        15                  20                  25

ACT GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GAA CTT   192
Thr Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Glu Leu
    30                  35                  40

GAA TGG TTG GGT TTT ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA GAC   240
Glu Trp Leu Gly Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr Asp
45                  50                  55                  60

TAC AGT GCA TCT GTG AAG GGT CGG TTC ACC ATC TCC AGA GAT AAT CCC   288
Tyr Ser Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Pro
                65                  70                  75

CAA AGC ATC CTC TAT CTT CAA ATG AAC ACC CTG ACA ACT GAG GAC AGT   336
Gln Ser Ile Leu Tyr Leu Gln Met Asn Thr Leu Thr Thr Glu Asp Ser
            80                  85                  90

GCC ACT TAT TAC TGT GCA AGA GAT AGG GGG GGG AGG GAC TGG TAC TTC   384
Ala Thr Tyr Tyr Cys Ala Arg Asp Arg Gly Gly Arg Asp Trp Tyr Phe
        95                  100                 105

GAT GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA GCC AAA ACG   432
Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys Thr
    110                 115                 120

ACA CCC                                                          438
Thr Pro
125
```

Sequence Listing

Seq. I.D. number : 4

Sequence length : 411

Sequence type : nucleic acid

Strandedn ss : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..411

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..30

Characteristics determination method : S

Sequence

```
CTT GTA ACA CGT TTA AAT GGT ATC CAG TGT GAG GTG AAG CTG GTG GAG    48
Leu Val Thr Arg Leu Asn Gly Ile Gln Cys Glu Val Lys Leu Val Glu
-10                 -5                  1                   5
TCT GGA GGA GGC TTG GTA CAG CCT GGG GGT TCT CTG AGA CTC TCC TGT    96
Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
                10                  15                  20
GCA ACT TCT GGG TTC ACC TTC ACT GAT TAC TAC ATG AAC TGG GTC CGC   144
Ala Thr Ser Gly Phe Thr Phe Thr Asp Tyr Tyr Met Asn Trp Val Arg
            25                  30                  35
CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG GGT TTT ATT AGA AAC AAA   192
Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu Gly Phe Ile Arg Asn Lys
        40                  45                  50
GCT AAT TAT TAC ACA ACA GAG TAC AGT GCA TCT GTG AAG GGT CGG TTC   240
Ala Asn Tyr Tyr Thr Thr Glu Tyr Ser Ala Ser Val Lys Gly Arg Phe
    55                  60                  65
ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC CTC TAT CTT CAA ATG AAC   288
Thr Ile Ser Arg Asp Asn Ser Gln Ser Ile Leu Tyr Leu Gln Met Asn
70                  75                  80                  85
ACC CTG AGA GCT GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA GAT GGG   336
Thr Leu Arg Ala Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg Asp Gly
                90                  95                  100
TTC CTA CGG GAC TGG TAC TTC GAT GTC TGG GGC GCA GGG ACC ACG GTC   384
Phe Leu Arg Asp Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val
            105                 110                 115

ACC GTC TCC TCA GCC AAA ACG ACA CCC                              411
Thr Val Ser Ser Ala Lys Thr Thr Pro
        120                 125
```

Sequence Listing

Seq. I.D. number : 5

Sequence length : 363

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..363

Characteristics determination method : S

Sequence

```
GAG GTT CAG CTC CAG CAG TCT GGG GCT GAA CTG GCA AGA CCT GGG GCT    48
Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
  1               5                  10                  15
TCA GTG AAC TTG TCC TGC AAG GCT TCT GGC TAC ACC TTT ACT AAC TAC    96
Ser Val Asn Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20                  25                  30
TGG ATG CAG TGG GTA AAA CAG AGG CGT GGA CAG GGT CTG GAA TGG ATT   144
Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45
GGG GCT ATT TAT CCT GGA GAT GGT GAT ACT AGG TAC ACT CAG AAG TTC   192
Gly Ala Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr Thr Gln Lys Phe
    50                  55                  60
AAG GGC AAG GCC ACA TTG ACT GCA GCT AAA TCC TCC AGC ACA GCC TAC   240
Lys Gly Lys Ala Thr Leu Thr Ala Ala Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75
ATG CAA CTC AGC AGC TTG GCA TCT GAG GAC TCT GCG GTC TAT TAC TGT   288
Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys
80                  85                  90                  95
GCA AGA TCG GGC TAC TAT GGT AGC TTC GTT GGG TTT GCT TAC TGG GGC   336
Ala Arg Ser Gly Tyr Tyr Gly Ser Phe Val Gly Phe Ala Tyr Trp Gly
            100                 105                 110
CAA GGG ACT CTG GTC ACT GTC TCT GCA                              363
Gln Gly Thr Leu Val Thr Val Ser Ala
        115                 120
```

Sequence Listing

Seq. I.D. number : 6

Sequence length : 354

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..354

Characteristics determination method : S

Sequence

```
GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CCT CTG    48
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Pro Leu
  1               5                  10                  15
GGG CAG AGG GCC ACC ATC TCA TAC AGG GCC AGC AAA AGT GTG CAG TTA    96
Gly Gln Arg Ala Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Gln Leu
            20                  25                  30
CAT CTG GCT ATA GTT TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG   144
His Leu Ala Ile Val Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln
        35                  40                  45
CCA CCC AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC   192
Pro Pro Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val
    50                  55                  60
CCT GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC   240
Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn
65                  70                  75
ATC CAT CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC   288
Ile His Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His
80                  85                  90                  95
ATT AGG GTA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA   336
Ile Arg Val Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
CGG GCT GAT GCT GCA CCA                                          354
Arg Ala Asp Ala Ala Pro
        115
```

Sequence Listing

Seq. I.D. number : 7

Sequence length : 438

Sequence type : nucl ic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..438

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..39

Characteristics determination method : S

Sequence

```
CTA TGG GTA CTG CTG CTC TGG GTT CCA GGT TCC ACT GGT GAC ATT GTG    48
Leu Trp Val Leu Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Ile Val
            -10                 -5                  1
CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG CAG AGG GCC    96
Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala
          5                  10                  15
TCC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAT AGT   144
Ser Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser
     20                  25                  30
TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG CCA CCC AGA CTC CTC   192
Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln Pro Pro Arg Leu Leu
 35                  40                  45                  50
ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC CCT GCC AGG TTC AGT   240
Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val Pro Ala Arg Phe Ser
                 55                  60                  65
GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG   288
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu
            70                  75                  80
GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT AGG GGA GCT TAC   336
Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Arg Gly Ala Tyr
        85                  90                  95
ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA CGG GCT GAT GCT GCA   384
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala Ala
    100                 105                 110
CCA ACT GTA TCC ATC TTC CCA CCA TCC AGT AAG CTT GGG AAA CGG TTC   432
Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Lys Leu Gly Lys Arg Phe
115                 120                 125                 130
GCA CCG                                                        438
Ala Pro
```

Sequ nce Listing
Seq. I.D. number : 8
Sequence length : 417
Sequence type : nucleic acid
Strandedness : double
Topology : linear
Sequence kind : mRNA
Original source
Organism : mouse
Sequence characteristics
Symbol expressing characteristics : CDS
Presence position : 28..417
Characteristics determination method : S
Symbol expressing characteristics : sig peptide
Presence position : 28..90
Characteristics determination method : S
Sequence

```
      GGCCGCG GTGAGAACCG TTGGGAATTC ATG GAG ACA GAC ACA CTC CTG    48
                                    Met Glu Thr Asp Thr Leu Leu
                                    -20                 -15
CTA TGG GTA CTG CTG CTC TGG GTT CCA GGT TCC ACT GGT GAC ATT GTG    96
Leu Trp Val Leu Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Ile Val
            -10                 -5                  1
CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG CAG AGG GCC   144
Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala
        5                   10                  15
ACC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAT AGT   192
Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser
    20                  25                  30
TAT ATG CAC TGG AAC CAA CAG AGA CCA GGA CAG CCA CCC AGA CTC CTC   240
Tyr Met His Trp Asn Gln Gln Arg Pro Gly Gln Pro Pro Arg Leu Leu
35                  40                  45                  50
ATC TAT CTT GTA TCC AAC CTA GAC TCT GGG GTC CCT GCC AGG TTC AGT   288
Ile Tyr Leu Val Ser Asn Leu Asp Ser Gly Val Pro Ala Arg Phe Ser
                55                  60                  65
GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG   336
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu
            70                  75                  80
GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT GAG GGA GCT TAC   384
Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Glu Gly Ala Tyr
        85                  90                  95
ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA                       417
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
    100                 105
```

Sequence Listing

Seq. I.D. number : 9

Sequence length : 420

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 31..420

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 31..90

Characteristics determination method : S

Sequence

```
      GCGGCCGCGG TGAGAACCGT TTGGGAATTC ATG GAG ACA CAG TCC CAG    48
                                       Met Glu Thr Gln Ser Gln
                                       -20                 -15
GTC TTT GTA TTC GTG TTT CTC TGG TTG TCT GGT GTT GAC GGA GAC ATT    96
Val Phe Val Phe Val Phe Leu Trp Leu Ser Gly Val Asp Gly Asp Ile
            -10                 -5                  1
GTG ATG ACC CAG TCT CAC AAA TTC ATG TCC ACA TCA GTA GGA GAC AGG   144
Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly Asp Arg
        5                   10                  15
GTC AGT ATC ACC TGC AAG GCC AGT CAG GAT GTG AAT ACT GCT GTA GCC   192
Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala Val Ala
    20                  25                  30
TGG TAT CAA CAG AAA CCA GGA CAA TCT CCT AAA CTA CTG CTT TAC TCG   240
Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Leu Tyr Ser
35                  40                  45
GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT CAC TTC ACT GGC AGT GGA   288
Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp His Phe Thr Gly Ser Gly
50                  55                  60                  65
TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC GGT GTG CAG GCT GAA GAC   336
Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Gly Val Gln Ala Glu Asp
                70                  75                  80
CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT AGT CCT CCT CTC ACG TTC   384
Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Pro Pro Leu Thr Phe
            85                  90                  95
GGT GCT GGG ACC AAG CTG GAA CTG AAA CGG GCT GAT                   420
Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala Asp
        100                 105
```

Sequence Listing

Seq. I.D. number : 10

Sequence length : 360

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..360

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..12

Characteristics determination method : S

Sequence

```
GGT GTT GAC GGA GAC ATT GTG ATG ACA CAG TCT CAC AAA TTC ATG TCC     48
Gly Val Asp Gly Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser
                 1               5                  10

ACA TCA GTT GGA GAC AGG GTC ACC ATC ACC TGC AAG GCC AGT CAG GAT     96
Thr Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp
            15                  20                  25

GTG ACT ACT GAT GTA GCC TGG TAT CAA CAG AAA CCA CGA CAA TCT CCT     144
Val Thr Thr Asp Val Ala Trp Tyr Gln Gln Lys Pro Arg Gln Ser Pro
        30                  35                  40

AAA CTA CTG ATT TAC TCG GCA TCC TAT CGG TAC ACT GGA GTC CCT GAT     192
Lys Leu Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp
    45                  50                  55

CGC TTC ACT GGC AGT GGA TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC     240
Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser
60                  65                  70                  75

AGT GTG CAG GCT GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT     288
Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr
                80                  85                  90

AGT ACT GCG TGG ACG TTC GGT GGT GGC ACC AAG CTG GAA ATC AAA CGG     336
Ser Thr Ala Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
            95                  100                 105

GCT GAT GCT GCA CCA ACT GTA TCC                                    360
Ala Asp Ala Ala Pro Thr Val Ser
        110                 115
```

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT:

(A) NAME:HAGIWARA, Yoshihide
(B) STREET:4-14, Hiraisanso
(C) CITY:Takarazuka-shi
(D) STATE:Hyogo-ken
(E) COUNTRY:Japan
(F) POSTAL CODE (ZIP):none

(ii) TITLE OF INVENTION:AMINO ACID SEQUENCES OF ANTI-IDIOTYPIC ANTIBODIES AGAINST ANTI-CANCER HUMAN MONOCLONAL ANTIBODY, AND DNA BASE SEQUENCES ENCODING THOSE SEQUENCES

(iii) NUMBER OF SEQUENCES:48

(iv) COMPUTER READABLE FORM:
(A) MEDIUM TYPE:Floppy disk
(B) COMPUTER:IBM PC compatible
(C) OPERATING SYSTEM:MS DOS 4.0
(D) SOFTWARE:Microsoft Word, Version 5.5

(v) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER:EP 94 115 683.8
(B) FILING DATE:October 5, 1994

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:5 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:H-CDR1-1
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:1:

Ser Tyr Trp Met His
5

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:5 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:H-CDR1-2
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 2:

Asp Tyr Tyr Met Asn
5

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:5 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:H-CDR1-3
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:3:

Asn Tyr Trp Met Gln
5

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:17 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:H-CDR2-1
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 4:

Ala Ile Tyr Pro Gly Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys
5 10 15
Asp

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:19 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:H-CDR2-2
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:5:

Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr Asp Tyr Ser Ala Ser
5 10 15
Val Lys Gly

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:19 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:

(A) NAME/KEY:H-CDR2-3
(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 6:

Phe Ile Arg Asn Lys Ala Asn Tyr Tyr Thr Thr Glu Tyr Ser Ala Ser
5 10 15
Val Lys Gly

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:17 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:H-CDR2-4
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:7:

Ala Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr Thr Glu Lys Phe Lys
5 10 15
Gly

(2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:10 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:H-CDR3-1
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 8:

Glu Glu Tyr Asp Tyr Asp Thr Leu Asp Tyr
5 10

(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:11 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:H-CDR3-2
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:9:

Asp Arg Gly Gly Arg Asp Trp Tyr Phe Asp Val
5 10

(2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:11 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:H-CDR3-3
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 10:

Asp Gly Phe Leu Arg Asp Trp Tyr Phe Asp Val
5 10

(2) INFORMATION FOR SEQ ID NO: 11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:12 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:H-CDR3-4
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:11:

Ser Gly Tyr Tyr Gly Ser Phe Val Gly Phe Ala Tyr
5 10

(2) INFORMATION FOR SEQ ID NO: 12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:17 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:L-CDR1-1
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 12:

Tyr Arg Ala Ser Lys Ser Val Gln Leu His Leu Ala Ile Val Tyr Met
5 10 15
His

(2) INFORMATION FOR SEQ ID NO: 13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:16 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:L-CDR1-2
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:13:

Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser Tyr Met His
5 10 15

(2) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:11 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:L-CDR1-3
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 14:

Lys Ala Ser Gln Asp Val Asn Thr Ala Val Ala
5 10

(2) INFORMATION FOR SEQ ID NO: 15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:11 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:L-CDR1-4
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:15:

Lys Ala Ser Gln Asp Val Thr Thr Asp Val Ala
5 10

(2) INFORMATION FOR SEQ ID NO: 16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:7 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:L-CDR2-1
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 16:

Leu Val Ser Asn Leu Glu Ser
5

(2) INFORMATION FOR SEQ ID NO: 17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:7 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:L-CDR2-2
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:17:

Leu Val Ser Asn Leu Asp Ser
5

(2) INFORMATION FOR SEQ ID NO: 18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:7 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:L-CDR2-3
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 18:

Ser Ala Ser Tyr Arg Tyr Thr
5

(2) INFORMATION FOR SEQ ID NO: 19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:8 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:L-CDR3-1
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:19:

Gln His Ile Arg Val Ala Tyr Thr
5

(2) INFORMATION FOR SEQ ID NO: 20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:8 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:L-CDR3-2
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 20:

Gln His Ile Arg Gly Ala Tyr Thr
5

(2) INFORMATION FOR SEQ ID NO: 21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:8 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:L-CDR3-3
(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:21:

Gln His Ile Glu Gly Ala Tyr Thr
5

(2) INFORMATION FOR SEQ ID NO: 22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:9 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:L-CDR3-4
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 22:

Gln Gln His Tyr Ser Pro Pro Leu Thr
5

(2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:9 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:L-CDR3-5
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:23:

Gln Gln His Tyr Ser Thr Ala Trp Thr
5

(2) INFORMATION FOR SEQ ID NO: 24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:34 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:single
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:cDNA
(iv) ANTISENSE:no
(iii) HYPOTHETICAL:no
(ix) FEATURE:
(A) NAME/KEY:H Leader Sequence A
(D) OTHER INFORMATION:R is A or G;
S is C or G;
K is G or T;
Y is C or T;
M is A or C.
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 24:

GGGAATTCAT GRASTTSKGG YYTMARCTKG RTTT 34

(2) INFORMATION FOR SEQ ID NO: 25:
(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:34 bas pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:single
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:cDNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(ix) FEATURE:
(A) NAME/KEY:H Leader Sequence B
(D) OTHER INFORMATION:S is C or G;
Y is C or T;
W is A or T;
R is A or G.
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:25:

GGGAATTCAT GRAATGSASC TGGGTYWTYC TCTT 34

(2) INFORMATION FOR SEQ ID NO: 26:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:18 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:single
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:cDNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(ix) FEATURE:
(A) NAME/KEY:H Leader Sequence C
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 26:

TTAAATGGTA TCCAGTGT 18

(2) INFORMATION FOR SEQ ID NO: 27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:35 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:single
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:cDNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(ix) FEATURE:
(A) NAME/KEY:H Constant Region
(D) OTHER INFORMATION:R is A or G;
K is G or T;
N is inosine.
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:27:

CCCAAGCTTC CAGGGRCCAR KGGATARACN GRTGG 35

(2) INFORMATION FOR SEQ ID NO: 28:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:32 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:single
(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:cDNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(ix) FEATURE:
(A) NAME/KEY:L Leader Sequence A
(D) OTHER INFORMATION:R is A or G;
K is G or T;
W is A or T;
Y is C or T.
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 28:

GGGAATTCAT GRAGWCACAK WCYCAGGTCT TT 32

(2) INFORMATION FOR SEQ ID NO: 29:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:33 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:single
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:cDNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(ix) FEATURE:
(A) NAME/KEY:L Leader Sequence B
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 29:

GGAATTCAAT GGAGACAGAC ACACTCCTGC TAT 33

(2) INFORMATION FOR SEQ ID NO: 30:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:30 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:single
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:cDNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(ix) FEATURE:
(A) NAME/KEY:L constant
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 30:

CCCAAGCTTA CTGGATGGTG GGAAGATGGA 30

(2) INFORMATION FOR SEQ ID NO: 31:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:357 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:double
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:mRNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(vi) ORIGINAL SOURCE:
(A) ORGANISM:mouse
(ix) FEATURE:

(A) NAME/KEY:Idio 3 H chain variable/Idio 17 H chain variable
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 31:

```
GAG GTT CAG CTC GAG CAG TCT GGG ACT GTG CTG GCA AGG CCT GGG GCT   48
Glu Val Gln Leu Gln Gln Ser Gly Thr Val Leu Ala Arg Pro Gly Ala
                5                   10                  15

TCA GTG AAG ATG TCC TGC AAG GCT TCG GGC TAC ACC TTT AAC AGC TAC   96
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Asn Ser Tyr
            20                  25                  30

TGG ATG CAC TGG GTA AAA CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT  144
Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

GGC GCG ATT TAT CCT GGA AAT AGT GAT ATT AGC TAC AGC CAG AAC TTT  192
Gly Ala Ile Tyr Pro Gly Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe
    50                  55                  60

AAG GAC AGG GCC AAA CTG ACT GCC GTC ACA TCC ACC AGC ACT GCC TAC  240
Lys Asp Arg Ala Lys Leu Thr Ala Val Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

ATG GAA CTC AGA AGC CTG ACA AAT GAG GAC TCT GCG GTC TAT TTC TGT  288
Met Glu Leu Arg Ser Leu Thr Asn Glu Asp Ser Ala Val Tyr Phe Cys
                85                  90                  95

ACA AAA GAG GAA TAT GAT TAC GAC ACC CTG GAC TAC TGG GGT CAA GGA  336
Thr Lys Glu Glu Tyr Asp Tyr Asp Thr Leu Asp Tyr Trp Gly Gln Gly
            100                 105                 110

ACC TCA GTC ACC GTC TCC TCA                                     357
Thr Ser Val Thr Val Ser Ser
        115
```

(2) INFORMATION FOR SEQ ID NO: 32:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:366 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:double
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:mRNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(vi) ORIGINAL SOURCE:
(A) ORGANISM:mouse
(ix) FEATURE:
(A) NAME/KEY:Idio 20 H chain variable
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 32:

```
GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG CCT GGG GGT   48
Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
                5                   10                  15

TCT CTC AGA CTC TCC TGT GCA ACT TCT GGG TTA ACC TTC ACT GAT TAC   96
Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Leu Thr Phe Thr Asp Tyr
            20                  25                  30
```

```
TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GAA CTT GAA TGG TTG  144
Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Glu Leu Glu Trp Leu
        35                  40                  45

GGT TTT ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA GAC TAC AGT GCA  192
Gly Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr Asp Tyr Ser Ala
    50                  55                  60

TCT GTG AAG GGT CGG TTC ACC ATC TCC AGA CAT AAT CCC CAA AGC ATC  240
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Pro Gln Ser Ile
65                  70                  75                  80

CTC TAT CTT CAA ATG AAC ACC CTG ACA ACT GAG GAC AGT GCC ACT TAT  288
Leu Tyr Leu Gln Met Asn Thr Leu Thr Thr Glu Asp Ser Ala Thr Tyr
                85                  90                  95

TAC TGT GCA AGA GAT AGG GGG GGG AGG GAC TGG TAC TTC GAT GTC TGG  336
Tyr Cys Ala Arg Asp Arg Gly Gly Arg Asp Trp Tyr Phe Asp Val Trp
            100                 105                 110

GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA                          366
Gly Ala Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

(2) INFORMATION FOR SEQ ID NO: 33:

(i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH:366 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:double
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:
- (A) ORGANISM:mouse

(ix) FEATURE:
- (A) NAME/KEY:Idio 27 H chain variable

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 33:

```
GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG CCT GGG GGT   48
Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
                5                   10                  15

TCT CTG AGA CTC TCC TGT GCA ACT TCT GGG TTC ACC TTC ACT GAT TAC   96
Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Phe Thr Phe Thr Asp Tyr
            20                  25                  30

TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG  144
Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu
        35                  40                  45

GGT TTT ATT AGA AAC AAA GCT AAT TAT TAC ACA ACA GAG TAC AGT GCA  192
Gly Phe Ile Arg Asn Lys Ala Asn Tyr Tyr Thr Thr Glu Tyr Ser Ala
    50                  55                  60
```

```
TCT GTG AAG GGT CGG TTC ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC  240
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Gln Ser Ile
65                  70                  75                  80

CTC TAT CTT CAA ATG AAC ACC CTG AGA GCT GAG GAC AGT GCC ACT TAT  288
Leu Gln Met Asn Thr Leu Thr Leu Arg Ala Glu Asp Ser Ala Thr Tyr
                85                  90                  95

TAC TGT GCA AGA GAT GGG TTC CTA CGG GAC TGG TAC TTC GAT GTC TGG  336
Tyr Cys Ala Arg Asp Gly Phe Leu Arg Asp Trp Tyr Phe Asp Val Trp
            100                 105                 110

GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA                          366
Gly Ala Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

(2) INFORMATION FOR SEQ ID NO: 34:

(i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH:363 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:double
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:
- (A) ORGANISM:mouse

(ix) FEATURE:
- (A) NAME/KEY:Idio 33 H chain variable

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 34:

```
GAG GTT CAG CTC CAG CAG TCT GGG GCT GAA CTG GCA AGA CCT GGG GCT   48
Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
                5                   10                  15

TCA GTG AAC TTG TCC TGC AAG GCT TCT GGC TAC ACC TTT ACT AAC TAC   96
Ser Val Asn Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20                  25                  30

TGG ATG CAG TGG GTA AAA CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT  144
Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

GGG GCT ATT TAT CCT GGA GAT GGT GAT ACT AGG TAC ACT CAG AAG TTC  192
Gly Ala Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr Thr Gln Lys Phe
    50                  55                  60

AAG GGC AAG GCC ACA TTG ACT GCA GCT AAA TCC TCC AGC ACA GCC TAC  240
Lys Gly Lys Ala Thr Leu Thr Ala Ala Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80

ATG CAA CTC AGC AGC TTG GCA TCT GAG GAC TCT GCG GTC TAT TAC TGT  288
Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85                  90                  95
```

```
GCA AGA TCG GGC TAC TAT GGT AGC TTC GTT GGG TTT GCT TAC TGG GGC  336
Ala Arg Ser Gly Tyr Tyr Gly Ser Phe Val Gly Phe Ala Tyr Trp Gly
            100                 105                 110

CAA GGG ACT CTG GTC ACT GTC TCT GCA                             363
Gln Gly Thr Leu Val Thr Val Ser Ala
        115                 120
```

(2) INFORMATION FOR SEQ ID NO: 35:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:336 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:double
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:mRNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(vi) ORIGINAL SOURCE:
(A) ORGANISM:mouse
(ix) FEATURE:
(A) NAME/KEY:Idio 3 L chain variable
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 35:

```
GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CCT CTG   48
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Pro Leu
                5                   10                  15

GGG CAG AGG GCC ACC ATC TCA TAC AGG GCC AGC AAA AGT GTG CAG TTA   96
Gly Gln Arg Ala Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Gln Leu
            20                  25                  30

CAT CTG GCT ATA GTT TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG  144
His Leu Ala Ile Val Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln
        35                  40                  45

CCA CCC AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC  192
Pro Pro Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val
    50                  55                  60

CCT GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC  240
Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn
65                  70                  75                  80

ATC CAT CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC  288
Ile His Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His
                85                  90                  95

ATT AGG GTA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA  336
Ile Arg Val Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

(2) INFORMATION FOR SEQ ID NO: 36:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:330 base pairs

(B) TYPE:nucleic acid
(C) STRANDEDNESS:double
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:mRNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(vi) ORIGINAL SOURCE:
(A) ORGANISM:mouse
(ix) FEATURE:
(A) NAME/KEY:Idio 17 L chain variable
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 36:

```
GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG   48
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
                 5                  10                  15

CAG AGG GCC TCC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT   96
Gln Arg Ala Ser Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser
            20                  25                  30

GGC TAT AGT TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG CCA CCC  144
Gly Tyr Ser Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln Pro Pro
        35                  40                  45

AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC CCT GCC  192
Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val Pro Ala
    50                  55                  60

AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT  240
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65                  70                  75                  80

CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT AGG  288
Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Arg
                85                  90                  95

GGA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA          330
Gly Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

(2) INFORMATION FOR SEQ ID NO: 37:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:330 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:double
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:mRNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(vi) ORIGINAL SOURCE:
(A) ORGANISM:mouse
(ix) FEATURE:
(A) NAME/KEY:Idio 20 L chain variable
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 37:

```
GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG   48
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
                 5                  10                  15

CAG AGG GCC ACC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT   96
Gln Arg Ala Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser
            20                  25                  30

GGC TAT AGT TAT ATG CAC TGG AAC CAA CAG AGA CCA GGA CAG CCA CCC  144
Gly Tyr Ser Tyr Met His Trp Asn Gln Gln Arg Pro Gly Gln Pro Pro
        35                  40                  45

AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAC TCT GGG GTC CCT GCC  192
Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Asp Ser Gly Val Pro Ala
    50                  55                  60

AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT  240
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65                  70                  75                  80

CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT GAG  288
Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Glu
                85                  90                  95

GGA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA          330
Gly Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

(2) INFORMATION FOR SEQ ID NO: 38:

(i) SEQUENCE CHARACTERISTICS:
  (A) LENGTH:321 base pairs
  (B) TYPE:nucleic acid
  (C) STRANDEDNESS:double
  (D) TOPOLOGY:linear
(ii) MOLECULE TYPE:mRNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(vi) ORIGINAL SOURCE:
  (A) ORGANISM:mouse
(ix) FEATURE:
  (A) NAME/KEY:Idio 27 L chain variable
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 38:

```
GAC ATT GTG ATG ACC CAG TCT CAC AAA TTC ATG TCC ACA TCA GTA GGA   48
Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
                 5                  10                  15

GAC AGG GTC AGT ATC ACC TGC AAG GCC AGT CAG GAT GTG AAT ACT GCT   96
Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala
            20                  25                  30

GTA GCC TGG TAT CAA CAG AAA CCA GGA CAA TCT CCT AAA CTA CTG CTT  144
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Leu
        35                  40                  45
```

```
TAC TCG GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT CAC TTC ACT GGC  192
Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp His Phe Thr Gly
    50                  55                  60

AGT GGA TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC GGT GTG CAG GCT  240
Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Gly Val Gln Ala
65                  70                  75                  80

GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT AGT CCT CCT CTC  288
Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Pro Pro Leu
                85                  90                  95

ACG TTC GGT GCT GGG ACC AAG CTG GAA CTG AAA                      321
Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO: 39:

(i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH:321 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:double
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:
- (A) ORGANISM:mouse

(ix) FEATURE:
- (A) NAME/KEY:Idio 33 L chain variable

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 39:

```
GAC ATT GTG ATG ACA CAG TCT CAC AAA TTC ATG TCC ACA TCA GTT GGA   48
Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
                5                   10                  15

GAC AGG GTC ACC ATC ACC TGC AAG GCC AGT CAG GAT GTG ACT ACT GAT   96
Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Thr Thr Asp
            20                  25                  30

GTA GCC TGG TAT CAA CAG AAA CCA CGA CAA TCT CCT AAA CTA CTG ATT  144
Val Ala Trp Tyr Gln Gln Lys Pro Arg Gln Ser Pro Lys Leu Leu Ile
        35                  40                  45

TAC TCG GCA TCC TAT CGG TAC ACT GGA GTC CCT GAT CGC TTC ACT GGC  192
Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
    50                  55                  60

AGT GGA TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC AGT GTG CAG GCT  240
Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Val Gln Ala
65                  70                  75                  80

GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT AGT ACT GCG TGG  288
Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Thr Ala Trp
                85                  90                  95
```

```
ACG TTC GGT GGT GGC ACC AAG CTG GAA ATC AAA                          321
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO: 40:

(i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH:399 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:double
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:
- (A) ORGANISM:mouse

(ix) FEATURE:
- (A) NAME/KEY:Clone 3GB1

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:40:

```
CTG TCG GTA ACT TCA GGG GTC TAC TCA GAG GTT CAG CTC GAG CAG TCT  -48
Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln Gln Ser
                -5                   1                   5

GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC AAG   96
Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys Lys
        10                  15                  20

GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA CAG  144
Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys Gln
    25                  30                  35

AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA AAT  192
Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
40                  45                  50                  55

AGT GAT ATT AGC TAC AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG ACT  240
Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu Thr
                60                  65                  70

GCC GTC ACA TCC ACC AGC ACT GCC TAC ATG GAA CTC AGA AGC CTG ACA  288
Ala Val Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr
            75                  80                  85

AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT TAC  336
Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asp Tyr
        90                  95                  100

GAC ACC CTG GAC TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TCC TCA  384
Asp Thr Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
    105                 110                 115

GCC AAA ACG ACA CCC                                             399
Ala Lys Thr Thr Pro
120
```

(2) INFORMATION FOR SEQ ID NO: 41:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:402 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:double
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:mRNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(vi) ORIGINAL SOURCE:
(A) ORGANISM:mouse
(ix) FEATURE:
(A) NAME/KEY:Clone 17GB7
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 41:

```
ATT GTG TCG GTA ACT TCA GGG GTC TAC TCA GAG GTT CAG CTC GAG CAG   48
Ile Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln Gln
-10                 -5                   1                   5

TCT GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC   96
Ser Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys
            10                  15                  20

AAG GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA  144
Lys Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys
        25                  30                  35

CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA  192
Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly
    40                  45                  50

AAT AGT GAT ATT AGC TAC AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG  240
Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu
55                  60                  65                  70

ACT GCC GTC ACA TCC ACC AGC ACT GCC TAC ATG GAA CTC AGA AGC CTG  288
Thr Ala Val Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu
                75                  80                  85

ACA AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT  336
Thr Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asp
            90                  95                  100

TAC GAC ACC CTG GAC TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TCC  384
Tyr Asp Thr Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
        105                 110                 115

TCA GCC AAA ACG ACA CCC                                         402
Ser Ala Lys Thr Thr Pro
    120
```

(2) INFORMATION FOR SEQ ID NO: 42:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:438 base pairs
(B) TYPE:nucleic acid

(C) STRANDEDNESS:double
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:mRNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(vi) ORIGINAL SOURCE:
(A) ORGANISM:mouse
(ix) FEATURE:
(A) NAME/KEY:Clone 20GA2
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:42:

```
ATG GAG TTC GGG CTA AAC TGG GTT TTC CTT GTA ACA CTT TTA AAT GGT   48
Met Glu Phe Gly Leu Asn Trp Val Phe Leu Val Thr Leu Leu Asn Gly
                -15                 -10                 -5

ATC CAG TGT GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG   96
Ile Gln Cys Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Gln
            1               5                  10

CCT GGG GGT TCT CTC AGA CTC TCC TGT GCA ACT TCT GGG TTA ACC TTC  144
Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Leu Thr Phe
    15                  20                  25

ACT GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GAA CTT  192
Thr Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Glu Leu
30                  35                  40                  45

GAA TGG TTG GGT TTT ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA GAC  240
Glu Trp Leu Gly Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr Asp
                50                  55                  60

TAC AGT GCA TCT GTG AAG GGT CGG TTC ACC ATC TCC AGA CAT AAT CCC  288
Tyr Ser Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Pro
            65                  70                  75

CAA AGC ATC CTC TAT CTT CAA ATG AAC ACC CTG ACA ACT GAG GAC AGT  336
Gln Ser Ile Leu Tyr Leu Gln Met Asn Thr Leu Thr Thr Glu Asp Ser
        80                  85                  90

GCC ACT TAT TAC TGT GCA AGA GAT AGG GGG GGG AGG GAC TGG TAC TTC  384
Ala Thr Tyr Tyr Cys Ala Arg Asp Arg Gly Gly Arg Asp Trp Tyr Phe
    95                  100                 105

GAT GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA GCC AAA ACG  432
Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys Thr
110                 115                 120                 125

ACA CCC                                                         438
Thr Pro
```

(2) INFORMATION FOR SEQ ID NO: 43:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:411 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:double
(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(vi) ORIGINAL SOURCE:
(A) ORGANISM:mouse
(ix) FEATURE:
(A) NAME/KEY:Clone 27GA5
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 43:

```
CTT GTA ACA CGT TTA AAT GGT ATC CAG TGT GAG GTG AAG CTG GTG GAG   48
Leu Val Thr Arg Leu Asn Gly Ile Gln Cys Glu Val Lys Leu Val Glu
-10                 -5                   1                   5

TCT GGA GGA GGC TTG GTA CAG CCT GGG GGT TCT CTG AGA CTC TCC TGT   96
Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
            10                  15                  20

GCA ACT TCT GGG TTC ACC TTC ACT GAT TAC TAC ATG AAC TGG GTC CGC  144
Ala Thr Ser Gly Phe Thr Phe Thr Asp Tyr Tyr Met Asn Trp Val Arg
        25                  30                  35

CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG GGT TTT ATT AGA AAC AAA  192
Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu Gly Phe Ile Arg Asn Lys
    40                  45                  50

GCT AAT TAT TAC ACA ACA GAG TAC AGT GCA TCT GTG AAG GGT CGG TTC  240
Ala Asn Tyr Tyr Thr Thr Glu Tyr Ser Ala Ser Val Lys Gly Arg Phe
55                  60                  65                  70

ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC CTC TAT CTT CAA ATG AAC  288
Thr Ile Ser Arg Asp Asn Ser Gln Ser Ile Leu Gln Met Asn Thr Leu
                75                  80                  85

ACC CTG AGA GCT GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA GAT GGG  336
Thr Leu Arg Ala Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg Asp Gly
            90                  95                  100

TTC CTA CGG GAC TGG TAC TTC GAT GTC TGG GGC GCA GGG ACC ACG GTC  384
Phe Leu Arg Asp Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val
        105                 110                 115

ACC GTC TCC TCA GCC AAA ACG ACA CCC                              411
Thr Val Ser Ser Ala Lys Thr Thr Pro
    120                 125
```

(2) INFORMATION FOR SEQ ID NO: 44:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:354 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:double
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:mRNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(vi) ORIGINAL SOURCE:
(A) ORGANISM:mouse

(ix) FEATURE:
(A) NAME/KEY:Clone 3KB11

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:44:

```
GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CCT CTG   48
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Pro Leu
                 5                  10                  15

GGG CAG AGG GCC ACC ATC TCA TAC AGG GCC AGC AAA AGT GTG CAG TTA   96
Gly Gln Arg Ala Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Gln Leu
            20                  25                  30

CAT CTG GCT ATA GTT TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG  144
His Leu Ala Ile Val Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln
        35                  40                  45

CCA CCC AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC  192
Pro Pro Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val
    50                  55                  60

CCT GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC  240
Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn
65                  70                  75                  80

ATC CAT CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC  288
Ile His Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His
                85                  90                  95

ATT AGG GTA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA  336
Ile Arg Val Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110

CGG GCT GAT GCT GCA CCA                                         354
Arg Ala Asp Ala Ala Pro
        115
```

(2) INFORMATION FOR SEQ ID NO: 45:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:438 base pairs
(B) TYPE:nucleic acid
(C) STANDEDNESS:double
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:mRNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(vi) ORIGINAL SOURCE:
(A) ORGANISM:mouse
(ix) FEATURE:
(A) NAME/KEY:Clone 17KB1
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 45:

```
CTA TGG GTA CTG CTG CTC TGG GTT CCA GGT TCC ACT GGT GAC ATT GTG   48
Leu Trp Val Leu Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Ile Val
            -10                 -5                  1
```

```
CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG CAG AGG GCC   96
Leu Thr Gln Ser Pro Ala Ser L u Ala Val Ser Leu Gly Gln Arg Ala
 5                  10                  15

TCC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAT AGT  144
Ser Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser
20                  25                  30                  35

TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG CCA CCC AGA CTC CTC  192
Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln Pro Pro Arg Leu Leu
                40                  45                  50

ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC CCT GCC AGG TTC AGT  240
Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val Pro Ala Arg Phe Ser
            55                  60                  65

GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG  288
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu
        70                  75                  80

GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT AGG GGA GCT TAC  336
Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Arg Gly Ala Tyr
    85                  90                  95

ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA CGG GCT GAT GCT GCA  384
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala Ala
100                 105                 110                 115

CCA ACT GTA TCC ATC TTC CCA CCA TCC AGT AAG CTT GGG AAA CGG TTC  432
Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Lys Leu Gly Lys Arg Phe
                120                 125                 130

GCA CCG                                                         438
Ala Pro
```

(2) INFORMATION FOR SEQ ID NO: 46:

(i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH:417 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:double
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:
- (A) ORGANISM:mouse

(ix) FEATURE:
- (A) NAME/KEY:Clone 20KB1

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:46:

```
     GGCCGCG GTGAGAACCG TTGGGAATTC ATG GAG ACA GAC ACA CTC CTG   48
                                   Met Glu Thr Asp Thr Leu Leu
                                   -20                 -15
```

```
CTA TGG GTA CTG CTG CTC TGG GTT CCA GGT TCC ACT GGT GAC ATT GTG   96
Leu Trp Val Leu Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Ile Val
            -10                 -5                  1

CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG CAG AGG GCC  144
Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala
         5                  10                  15

ACC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAT AGT  192
Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser
        20                  25                  30

TAT ATG CAC TGG AAC CAA CAG AGA CCA GGA CAG CCA CCC AGA CTC CTC  240
Tyr Met His Trp Asn Gln Gln Arg Pro Gly Gln Pro Pro Arg Leu Leu
    35                  40                  45

ATC TAT CTT GTA TCC AAC CTA GAC TCT GGG GTC CCT GCC AGG TTC AGT  288
Ile Tyr Leu Val Ser Asn Leu Asp Ser Gly Val Pro Ala Arg Phe Ser
50                  55                  60                  65

GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG  336
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu
                70                  75                  80

GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT GAG GGA GCT TAC  384
Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Glu Gly Ala Tyr
            85                  90                  95

ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA                      417
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
        100                 105
```

(2) INFORMATION FOR SEQ ID NO: 47:

(i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH:420 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:single
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:
- (A) ORGANISM:mouse

(ix) FEATURE:
- (A) NAME/KEY:Clone 27KA2

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 47:

```
      GCGGCCGCGG TGAGAACCGT TTGGGAATTC ATC GAG ACA CAG TCC CAG   48
                                       Met Glu Thr Gln Ser Gln
                                       -20                 -15

GTC TTT GTA TTC GTG TTT CTC TGG TTG TCT GGT GTT GAC GGA GAC ATT   96
Val Phe Val Phe Val Phe Leu Trp Leu Ser Gly Val Asp Gly Asp Ile
                -10                 -5                  1
```

```
GTG ATG ACC CAG TCT CAC AAA TTC ATG TCC ACA TCA GTA GGA GAC AGG  144
Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly Asp Arg
 5                  10                  15

GTC AGT ATC ACC TGC AAG GCC AGT CAG GAT GTG AAT ACT GCT GTA GCC  192
Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala Val Ala
     20                  25                  30

TGG TAT CAA CAG AAA CCA GGA CAA TCT CCT AAA CTA CTG CTT TAC TCG  240
Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Leu Tyr Ser
 35                  40                  45                  50

GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT CAC TTC ACT GGC AGT GGA  288
Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp His Phe Thr Gly Ser Gly
                 55                  60                  65

TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC GGT GTG CAG GCT GAA GAC  336
Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Gly Val Gln Ala Glu Asp
             70                  75                  80

CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT AGT CCT CCT CTC ACG TTC  384
Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Pro Pro Leu Thr Phe
         85                  90                  95

GGT GCT GGG ACC AAG CTG GAA CTG AAA CGG GCT GAT                  420
Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala Asp
     100                 105                 110
```

(2) INFORMATION FOR SEQ ID NO: 48:

(i) SEQUENCE CHARACTERISTICS:
  (A) LENGTH:360 base pairs
  (B) TYPE:nucleic acid
  (C) STRANDEDNESS:single
  (D) TOPOLOGY:linear
(ii) MOLECULE TYPE:mRNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(vi) ORIGINAL SOURCE:
  (A) ORGANISM:mouse
(ix) FEATURE:
  (A) NAME/KEY:Clone 23KA26
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:48

```
GGT GTT GAC GGA GAC ATT GTG ATG ACA CAG TCT CAC AAA TTC ATG TCC   48
Gly Val Asp Gly Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser
                 1                   5                  10

ACA TCA GTT GGA GAC AGG GTC ACC ATC ACC TGC AAG GCC AGT CAG GAT   96
Thr Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp
             15                  20                  25

GTG ACT ACT GAT GTA GCC TGG TAT CAA CAG AAA CCA CGA CAA TCT CCT  144
Val Thr Thr Asp Val Ala Trp Tyr Gln Gln Lys Pro Arg Gln Ser Pro
         30                  35                  40
```

```
AAA CTA CTG ATT TAC TCG GCA TCC TAT CGG TAC ACT GGA GTC CCT GAT  192
Lys Leu Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp
    45                  50                  55

CGC TTC ACT GGC AGT GGA TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC  240
Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser
60                  65                  70                  75

AGT GTG CAG GCT GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT  288
Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr
                80                  85                  90

AGT ACT GCG TGG ACG TTC GGT GGT GGC ACC AAG CTG GAA ATC AAA CCG  336
Ser Thr Ala Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
            95                  100                 105

GCT GAT GCT GCA CCA ACT GTA TCC                                  360
Ala Asp Ala Ala Pro Thr Val Ser
        110                 115
```

Claims

1. An immunoglobulin H chain variable region fragment which contains a hypervariable region CDR1 having an amino acid sequence selected from

(1) Ser Tyr Trp Met His;
Asp Tyr Tyr Met Asn; and
Asn Tyr Trp Met Gln,

a hypervariable region CDR2 having an amino acid sequence selected from

(2) Ala Ile Tyr Pro Gly Asn Ser
Asp Ile Ser Tyr Ser Gln Asn
Phe Lys Asp;
Phe Ile Arg Asn Lys Ala
Asn Leu Tyr Thr Thr Asp
Tyr Ser Ala Ser Val Lys
Gly;
Phe Ile Arg Asn Lys Ala
Asn Tyr Tyr Thr Thr Glu
Tyr Ser Ala Ser Val Lys
Gly; and
Ala Ile Tyr Pro Gly Asp
Gly Asp Thr Arg Tyr Thr
Gln Lys Phe Lys Gly,

and a hypervariable region CDR3 having an amino acid sequenc selected from

(3) Glu Glu Tyr Asp Tyr Asp
Thr Leu Asp Tyr;
Asp Arg Gly Gly Arg Asp
Trp Tyr Phe Asp Val;
Asp Gly Phe Leu Arg Asp
Trp Tyr Phe Asp Val; and
Ser Gly Tyr Tyr Gly Ser
Phe Val Gly Phe Ala Tyr .

2. An immunoglobulin H chain variable region fragment having the following amino acid sequence

Glu Val Gln Leu Gln Gln Ser Gly Thr Val
Leu Ala Arg Pro Gly Ala Ser Val Lys Met
Ser Cys Lys Ala Ser Gly Tyr Thr Phe Asn
Ser Tyr Trp Met His Trp Val Lys Gln Arg
Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala
Ile Tyr Pro Gly Asn Ser Asp Ile Ser Tyr
Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu
Thr Ala Val Thr Ser Thr Ser Thr Ala Tyr
Met Glu Leu Arg Ser Leu Thr Asn Glu Asp
Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu
Tyr Asp Tyr Asp Thr Leu Asp Tyr Trp Gly
Gln Gly Thr Ser Val Thr Val Ser Ser.

3. An immunoglobulin H chain variable region fragment having the following amino acid sequence

Glu Val Lys Leu Val Glu Ser Gly Gly Gly
Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
Ser Cys Ala Thr Ser Gly Phe Thr Phe Thr
Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro
Pro Gly Lys Ala Leu Glu Trp Leu Gly Phe
Ile Arg Asn Lys Ala Asn Tyr Tyr Thr Thr
Glu Tyr Ser Ala Ser Val Lys Gly Arg Phe
Thr Ile Ser Arg Asp Asn Ser Gln Ser Ile
Leu Tyr Leu Gln Met Asn Thr Leu Arg Ala
Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg
Asp Gly Phe Leu Arg Asp Trp Tyr Phe Asp
Val Trp Gly Ala Gly Thr Thr Val Thr Val
Ser Ser.

4. An immunoglobulin H chain variable region fragment having the following amino acid sequence

Glu Val Lys Leu Val Glu Ser Gly Gly Gly
Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
Ser Cys Ala Thr Ser Gly Leu Thr Phe Thr
Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro
Pro Gly Lys Glu Leu Glu Trp Leu Gly Phe
Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr
Asp Tyr Ser Ala Ser Val Lys Gly Arg Phe
Thr Ile Ser Arg Asp Asn Pro Gln Ser Ile
Leu Tyr Leu Gln Met Asn Thr Leu Thr Thr
Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg
Asp Arg Gly Gly Arg Asp Trp Tyr Phe Asp
Val Trp Gly Ala Gly Thr Thr Val Thr Val
Ser Ser.

5. An immunoglobulin H chain variabl region fragment having the following amino acid sequenc

Glu Val Gln Leu Gln Gln Ser Gly Ala Glu
Leu Ala Arg Pro Gly Ala Ser Val Asn Leu
Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr
Asn Tyr Trp Met Gln Trp Val Lys Gln Arg
Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala
Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr
Thr Gln Lys Phe Lys Gly Lys Ala Thr Leu
Thr Ala Ala Lys Ser Ser Ser Thr Ala Tyr
Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
Ser Ala Val Tyr Tyr Cys Ala Arg Ser Gly
Tyr Tyr Gly Ser Phe Val Gly Phe Ala Tyr
Trp Gly Gln Gly Thr Leu Val Thr Val Ser
Ala .

6. DNA and RNA fragments each encoding an immunoglobulin H chain variable region fragment which contains a base sequence encoding a hypervariable region CDR1 having an amino acid sequence selected from

(1) Ser Tyr Trp Met His;
Asp Tyr Tyr Met Asn; and
Asn Tyr Trp Met Gln ,

a base sequence encoding a hypervariable region CDR2 having an amino acid sequence selected from

(2) Ala Ile Tyr Pro Gly Asn Ser
Asp Ile Ser Tyr Ser Gln Asn
Phe Lys Asp;
Phe Ile Arg Asn Lys Ala
Asn Leu Tyr Thr Thr Asp
Tyr Ser Ala Ser Val Lys
Gly;
Phe Ile Arg Asn Lys Ala
Asn Tyr Tyr Thr Thr Glu
Tyr Ser Ala Ser Val Lys
Gly; and
Ala Ile Tyr Pro Gly Asp
Gly Asp Thr Arg Tyr Thr
Glu Lys Phe Lys Gly ,

a base sequence encoding a hypervariable region CDR3 having an amino acid sequence selected from

(3) Glu Glu Tyr Asp Tyr Asp
Thr Leu Asp Tyr;
Asp Arg Gly Gly Arg Asp
Trp Tyr Phe Asp Val;
Asp Gly Phe Leu Arg Asp
Trp Tyr Phe Asp Val; and
Ser Gly Tyr Tyr Gly Ser
Phe Val Gly Phe Ala Tyr .

7. An immunoglobulin H chain variable region fragment having following base sequence

GAG GTT CAG CTC CAG CAG TCT GGG ACT GTG
CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG
TCC TGC AAG GCT TCG GGC TAC ACC TTT AAC
AGC TAC TGG ATG CAC TGG GTA AAA CAG AGG
CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG
ATT TAT CCT GGA AAT AGT GAT ATT AGC TAC
AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG
ACT GCC GTC ACA TCC ACC AGC ACT GCC TAC
ATG GAA CTC AGA AGC CTG ACA AAT GAG GAC
TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA
TAT GAT TAC GAC ACC CTG GAC TAC TGG GGT
CAA GGA ACC TCA GTC ACC GTC TCC TCA.

8. An immunoglobulin H chain variable region fragm nt having the following base sequence

GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC
TTG GTA CAG CCT GGG GGT TCT CTC AGA CTC
TCC TGT GCA ACT TCT GGG TTA ACC TTC ACT
GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT
CCA GGA AAG GAA CTT GAA TGG TTG GGT TTT
ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA
GAC TAC AGT GCA TCT GTG AAG GGT CGG TTC
ACC ATC TCC AGA GAT AAT CCC CAA AGC ATC
CTC TAT CTT CAA ATG AAC ACC CTG ACA ACT
GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA
GAT AGG GGG GGG AGG GAC TGG TAC TTC GAT
GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC
TCC TCA .

9. An immunoglobulin H chain variable region fragment having the following base sequence

GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC
TTG GTA CAG CCT GGG GGT TCT CTG AGA CTC
TCC TGT GCA ACT TCT GGG TTC ACC TTC ACT
GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT
CCA GGA AAG GCA CTT GAG TGG TTG GGT TTT
ATT AGA AAC AAA GCT AAT TAT TAC ACA ACA
GAG TAC AGT GCA TCT GTG AAG GGT CGG TTC
ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC
CTC TAT CTT CAA ATG AAC ACC CTG AGA GCT
GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA
GAT GGG TTC CTA CGG GAC TGG TAC TTC GAT
GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC
TCC TCA.

10. An immunoglobulin H chain variable region fragment having the following base sequence

GAG GTT CAG CTC CAG CAG TCT GGG GCT GAA
CTG GCA AGA CCT GGG GCT TCA GTG AAC TTG
TCC TGC AAG GCT TCT GGC TAC ACC TTT ACT
AAC TAC TGG ATG CAG TGG GTA AAA CAG AGG
CCT GGA CAG GGT CTG GAA TGG ATT GGG GCT
ATT TAT CCT GGA GAT GGT GAT ACT AGG TAC
ACT CAG AAG TTC AAG GGC AAG GCC ACA TTG
ACT GCA GCT AAA TCC TCC AGC ACA GCC TAC
ATG CAA CTC AGC AGC TTG GCA TCT GAG GAC
TCT GCG GTC TAT TAC TGT GCA AGA TCG GGC
TAC TAT GGT AGC TTC GTT GGG TTT GCT TAC
TGG GGC CAA GGG ACT CTG GTC ACT GTC TCT
GCA .

11. An immunoglobulin L chain variable region fragment which contains a hypervariable region CDR1 having an amino acid sequence selected from

(1) Tyr Arg Ala Ser Lys Ser Val
Gln Leu His Leu Ala Ile Val
Tyr Met His;
Tyr Arg Ala Ser Lys Ser Val
Ser Thr Ser Gly Tyr Ser Tyr
Met His;
Lys Ala Ser Gln Asp Val Asn
Thr Ala Val Ala; and
Lys Ala Ser Gln Asp Val Thr
Thr Asp Val Ala ,

a hypervariable region CDR2 having an amino acid sequence selected from

(2) Leu Val Ser Asn Leu Glu Ser;
Leu Val Ser Asn Leu Asp Ser; and
Ser Ala Ser Tyr Arg Tyr Thr,

and a hypervariable region CDR3 having an amino acid sequence selected from

(3) Gln His Ile Arg Val Ala Tyr Thr;
Gln His Ile Arg Gly Ala Tyr Thr;
Gln His Ile Glu Gly Ala Tyr Thr;
Gln Gln His Tyr Ser Pro Pro Leu Thr; and
Gln Gln His Tyr Ser Thr Ala Trp Thr .

12. An immunoglobulin L chain variable region fragment having the following amino acid sequence

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser
Leu Ala Val Ser Pro Leu Gly Gln Arg Ala
Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val
Gln Leu His Leu Ala Ile Val Tyr Met His
Trp Asn Gln Gln Lys Pro Gly Gln Pro Pro
Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu
Glu Ser Gly Val Pro Ala Arg Phe Ser Gly
Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn
Ile His Pro Val Glu Glu Glu Asp Ala Ala
Thr Tyr Tyr Cys Gln His Ile Arg Val Ala
Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu
Ile Lys .

13. An immunoglobulin L chain variabl region fragment having the following amino acid sequence

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser
Leu Ala Val Ser Leu Gly Gln Arg Ala Ser
Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser
Thr Ser Gly Tyr Ser Tyr Met His Trp Asn
Gln Gln Lys Pro Gly Gln Pro Pro Arg Leu
Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser
Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
Ser Gly Thr Asp Phe Thr Leu Asn Ile His
Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr
Tyr Cys Gln His Ile Arg Gly Ala Tyr Thr
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys.

14. An immunoglobulin L chain variable region fragment having the following amino acid sequence

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser
Leu Ala Val Ser Leu Gly Gln Arg Ala Thr
Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser
Thr Ser Gly Tyr Ser Tyr Met His Trp Asn
Gln Gln Arg Pro Gly Gln Pro Pro Arg Leu
Leu Ile Tyr Leu Val Ser Asn Leu Asp Ser
Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
Ser Gly Thr Asp Phe Thr Leu Asn Ile His
Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr
Tyr Cys Gln His Ile Glu Gly Ala Tyr Thr
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys.

15. An immunoglobulin L chain variable region fragment having the following amino acid sequenc

Asp Ile Val Met Thr Gln Ser His Lys Phe
Met Ser Thr Ser Val Gly Asp Arg Val Ser
Ile Thr Cys Lys Ala Ser Gln Asp Val Asn
Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro
Gly Gln Ser Pro Lys Leu Leu Leu Tyr Ser
Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp
His Phe Thr Gly Ser Gly Ser Gly Thr Asp
Phe Thr Phe Thr Ile Ser Gly Val Gln Ala
Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln
His Tyr Ser Pro Pro Leu Thr Phe Gly Ala
Gly Thr Lys Leu Glu Leu Lys .

16. An immunoglobulin L chain variable region fragment having the following amino acid sequence

Asp Ile Val Met Thr Gln Ser His Lys Phe
Met Ser Thr Ser Val Gly Asp Arg Val Thr
Ile Thr Cys Lys Ala Ser Gln Asp Val Thr
Thr Asp Val Ala Trp Tyr Gln Gln Lys Pro
Arg Gln Ser Pro Lys Leu Leu Ile Tyr Ser
Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp
Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp
Phe Thr Phe Thr Ile Ser Ser Val Gln Ala
Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln
His Tyr Ser Thr Ala Trp Thr Phe Gly Gly
Gly Thr Lys Leu Glu Ile Lys .

17. DNA and RNA fragments each encoding an immunoglobulin L chain variable region fragment which contains a bas sequence encoding a hypervariable region CDR1 having an amino acid sequence selected from

(1) Tyr Arg Ala Ser Lys Ser Val Gln Leu His Leu Ala Ile Val Tyr Met His;
Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser Tyr Met His;
Lys Ala Ser Gln Asp Val Asn Thr Ala Val Ala; and
Lys Ala Ser Gln Asp Val Thr Thr Asp Val Ala ,

a base sequence encoding a hypervariable region CDR2 having an amino acid sequence selected from

(2) Leu Val Ser Asn Leu Glu Ser;
Leu Val Ser Asn Leu Asp Ser; and
Ser Ala Ser Tyr Arg Tyr Thr ,

and a base sequence encoding a hypervariable region CDR3 having an amino acid sequence selected from

(3) Gln His Ile Arg Val Ala Tyr Thr;
Gln His Ile Arg Gly Ala Tyr Thr;
Gln His Ile Glu Gly Ala Tyr Thr;
Gln Gln His Tyr Ser Pro Pro Leu Thr; and
Gln Gln His Tyr Ser Thr Ala Trp Thr .

18. An immunoglobulin L chain variable region fragment having the following base sequence

GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC
TTA GCT GTA TCT CCT CTG GGG CAG AGG GCC
ACC ATC TCA TAC AGG GCC AGC AAA AGT GTG
CAG TTA CAT CTG GCT ATA GTT TAT ATG CAC
TGG AAC CAA CAG AAA CCA GGA CAG CCA CCC
AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA
GAA TCT GGG GTC CCT GCC AGG TTC AGT GGC
AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC
ATC CAT CCT GTG GAG GAG GAG GAT GCT GCA
ACC TAT TAC TGT CAG CAC ATT AGG GTA GCT
TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA
ATA AAA .

19. An immunoglobulin L chain variable region fragment having the following base sequence

GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC
TTA GCT GTA TCT CTG GGG CAG AGG GCC TCC
ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT
ACA TCT GGC TAT AGT TAT ATG CAC TGG AAC
CAA CAG AAA CCA GGA CAG CCA CCC AGA CTC
CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT
GGG GTC CCT GCC AGG TTC AGT GGC AGT GGG
TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT
CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT
TAC TGT CAG CAC ATT AGG GGA GCT TAC ACG
TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA .

20. An immunoglobulin L chain variable region fragment having the following base sequence

GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC
TTA GCT GTA TCT CTG GGG CAG AGG GCC ACC
ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT
ACA TCT GGC TAT AGT TAT ATG CAC TGG AAC
CAA CAG AGA CCA GGA CAG CCA CCC AGA CTC
CTC ATC TAT CTT GTA TCC AAC CTA GAC TCT
GGG GTC CCT GCC AGG TTC AGT GGC AGT GGG
TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT
CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT
TAC TGT CAG CAC ATT GAG GGA GCT TAC ACG
TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA .

21. An immunoglobulin L chain variable region fragment having the following base sequence

GAC ATT GTG ATG ACC CAG TCT CAC AAA TTC
ATG TCC ACA TCA GTA GGA GAC AGG GTC AGT
ATC ACC TGC AAG GCC AGT CAG GAT GTG AAT
ACT GCT GTA GCC TGG TAT CAA CAG AAA CCA
GGA CAA TCT CCT AAA CTA CTG CTT TAC TCG
GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT
CAC TTC ACT GGC AGT GGA TCT GGG ACG GAT
TTC ACT TTC ACC ATC AGC GGT GTG CAG GCT
GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA
CAT TAT AGT CCT CCT CTC ACG TTC GGT GCT
GGG ACC AAG CTG GAA CTG AAA .

22. An immunoglobulin L chain variable region fragment having the following base sequence

GAC ATT GTG ATG ACA CAG TCT CAC AAA TTC
ATG TCC ACA TCA GTT GGA GAC AGG GTC ACC
ATC ACC TGC AAG GCC AGT CAG GAT GTG ACT
ACT GAT GTA GCC TGG TAT CAA CAG AAA CCA
CGA CAA TCT CCT AAA CTA CTG ATT TAC TCG
GCA TCC TAT CGG TAC ACT GGA GTC CCT GAT
CGC TTC ACT GGC AGT GGA TCT GGG ACG GAT
TTC ACT TTC ACC ATC AGC AGT GTG CAG GCT
GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA
CAT TAT AGT ACT GCG TGG ACG TTC GGT GGT
GGC ACC AAG CTG GAA ATC AAA .

23. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 2 and the immunoglobulin L chain variable region fragment according to claim 12.

24. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 2 and the immunoglobulin L chain variable region fragment according to claim 13.

25. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 3 and the immunoglobulin L chain variable region fragment according to claim 14.

26. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 4 and the immunoglobulin L chain variable region fragment according to claim 15.

27. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 5 and the immunoglobulin L chain variable region fragment according to claim 16.

FIG. 1

Idio 3	+	λ	K	G3	G2b	G2a	G1	M	A
Idio 17	+	λ	K	G3	G2b	G2a	G1	M	A
Idio 20	+	λ	K	G3	G2b	G2a	G1	M	A
Idio 27	+	λ	K	G3	G2b	G2a	G1	M	A
Idio 33	+	λ	K	G3	G2b	G2a	G1	M	A

FIG. 2

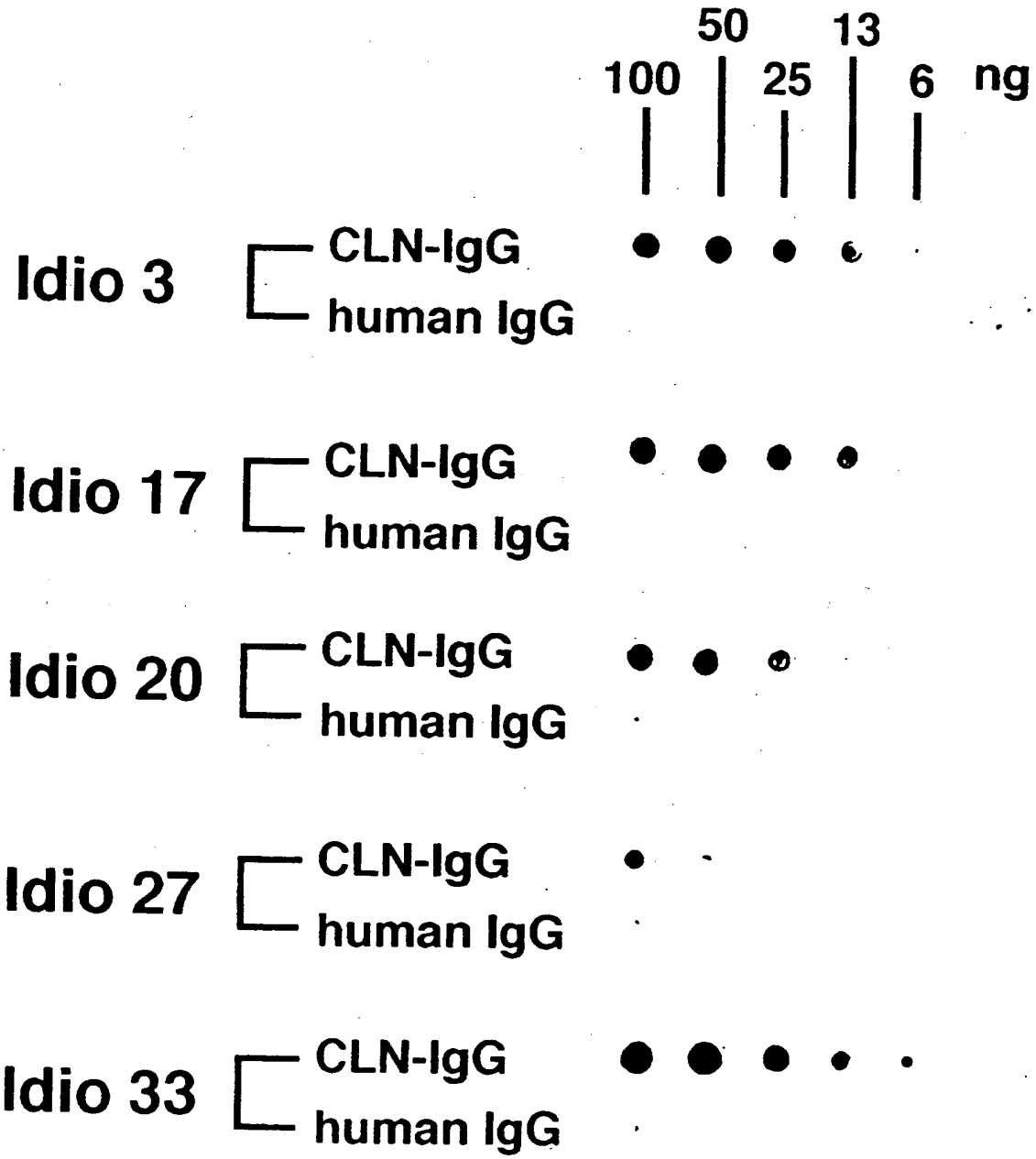
100
50
25
13
6
ng
Idio 3
CLN-IgG
human IgG
Idio 17
CLN-IgG
human IgG
Idio 20
CLN-IgG
human IgG
Idio 27
CLN-IgG
human IgG
Idio 33
CLN-IgG
human IgG

FIG. 3

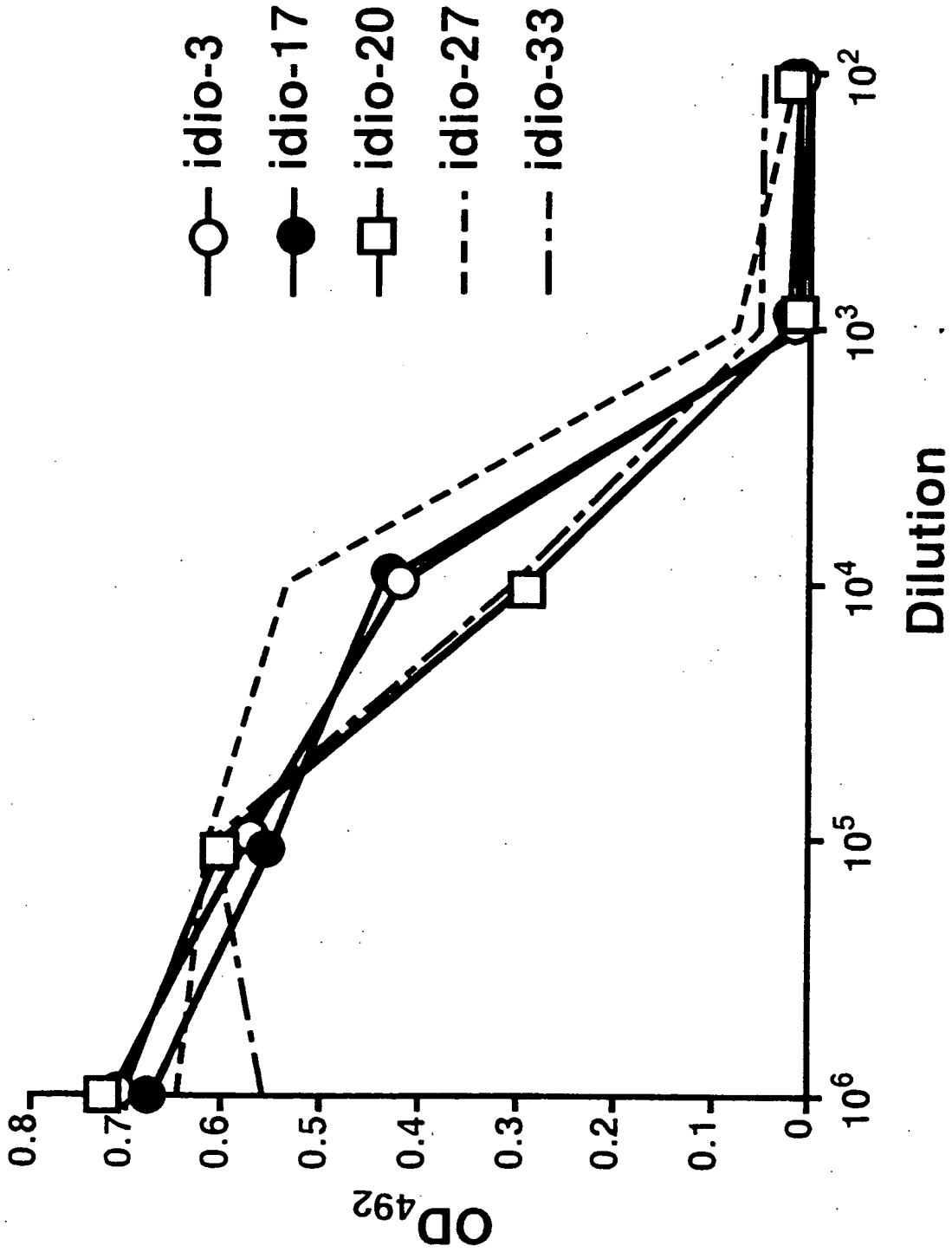
idio-3
idio-17
idio-20
idio-27
idio-33
OD492
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Dilution
10^2
10^3
10^4
10^5
10^6

FIG. 4

		3	17	20	27	33
FR1	1	Glu	Glu	Glu	Glu	Glu
	2	Val	Val	Val	Val	Val
	3	Gln	Gln	Lys	Lys	Gln
	4	Leu	Leu	Leu	Leu	Leu
	5	Gln	Gln	Val	Val	Gln
	6	Gln	Gln	Glu	Glu	Gln
	7	Ser	Ser	Ser	Ser	Ser
	8	Gly	Gly	Gly	Gly	Gly
	9	Thr	Thr	Gly	Gly	Ala
	10	Val	Val	Gly	Gly	Glu
	11	Leu	Leu	Leu	Leu	Leu
	12	Ala	Ala	Val	Val	Ala
	13	Arg	Arg	Gln	Gln	Arg
	14	Pro	Pro	Pro	Pro	Pro
	15	Gly	Gly	Gly	Gly	Gly
	16	Ala	Ala	Gly	Gly	Ala
	17	Ser	Ser	Ser	Ser	Ser
	18	Val	Val	Leu	Leu	Val
	19	Lys	Lys	Arg	Arg	Asn
	20	Met	Met	Leu	Leu	Leu
	21	Ser	Ser	Ser	Ser	Ser
	22	Cys	Cys	Cys	Cys	Cys
	23	Lys	Lys	Ala	Ala	Lys
	24	Ala	Ala	Thr	Thr	Ala
	25	Ser	Ser	Ser	Ser	Ser
	26	Gly	Gly	Gly	Gly	Gly
	27	Tyr	Tyr	Leu	Phe	Tyr
	28	Thr	Thr	Thr	Thr	Thr
	29	Phe	Phe	Phe	Phe	Phe
	30	Asn	Asn	Thr	Thr	Thr
CDR1	31	Ser	Ser	Asp	Asp	Asn
	32	Tyr	Tyr	Tyr	Tyr	Tyr
	33	Trp	Trp	Tyr	Tyr	Trp
	34	Met	Met	Met	Met	Met
FR2	35	His	His	Asn	Asn	Gln
	36	Trp	Trp	Trp	Trp	Trp
	37	Val	Val	Val	Val	Val
	38	Lys	Lys	Arg	Arg	Lys
	39	Gln	Gln	Gln	Gln	Gln
	40	Arg	Arg	Pro	Pro	Arg
	41	Pro	Pro	Pro	Pro	Pro
	42	Gly	Gly	Gly	Gly	Gly
	43	Gln	Gln	Lys	Lys	Gln
	44	Gly	Gly	Glu	Ala	Gly
	45	Leu	Leu	Leu	Leu	Leu
	46	Glu	Glu	Glu	Glu	Glu
	47	Trp	Trp	Trp	Trp	Trp
	48	Ile	Ile	Leu	Leu	Ile
CDR2	49	Gly	Gly	Gly	Gly	Gly
	50	Ala	Ala	Phe	Phe	Ala
	51	Ile	Ile	Ile	Ile	Ile
	52	Tyr	Tyr	Arg	Arg	Tyr
	52A	Pro	Pro	Asn	Asn	Pro
	52B	---	---	Lys	Lys	---
	52C	---	---	Ala	Ala	---
	53	Gly	Gly	Asn	Asn	Gly
	54	Asn	Asn	Leu	Tyr	Asp
	55	Ser	Ser	Tyr	Tyr	Gly
	56	Asp	Asp	Thr	Thr	Asp
	57	Ile	Ile	Thr	Thr	Thr
	58	Ser	Ser	Asp	Glu	Arg
	59	Tyr	Tyr	Tyr	Tyr	Tyr
	60	Ser	Ser	Ser	Ser	Thr
	61	Gln	Gln	Ala	Ala	Gln
	62	Asn	Asn	Ser	Ser	Lys
	63	Phe	Phe	Val	Val	Phe
	64	Lys	Lys	Lys	Lys	Lys
	65	Asp	Asp	Gly	Gly	Gly
	66	Arg	Arg	Arg	Arg	Lys
	67	Ala	Ala	Phe	Phe	Ala
FR3	68	Lys	Lys	Thr	Thr	Thr
	69	Leu	Leu	Ile	Ile	Leu
	70	Thr	Thr	Ser	Ser	Thr
	71	Ala	Ala	Arg	Arg	Ala
	72	Val	Val	Asp	Asp	Ala
	73	Thr	Thr	Asn	Asn	Lys
	74	Ser	Ser	Pro	Ser	Ser
	75	Thr	Thr	Gln	Gln	Ser
	76	Ser	Ser	Ser	Ser	Ser
	77	Thr	Thr	Ile	Ile	Thr
	78	Ala	Ala	Leu	Leu	Ala
	79	Tyr	Tyr	Tyr	Tyr	Tyr
	80	Met	Met	Leu	Leu	Met
	81	Glu	Glu	Gln	Gln	Gln
	82	Leu	Leu	Met	Met	Leu
	82A	Arg	Arg	Asn	Asn	Ser
	82B	Ser	Ser	Thr	Thr	Ser
	82C	Leu	Leu	Leu	Leu	Leu
	83	Thr	Thr	Thr	Arg	Ala
	84	Asn	Asn	Thr	Ala	Ser
	85	Glu	Glu	Glu	Glu	Glu
	86	Asp	Asp	Asp	Asp	Asp
	87	Ser	Ser	Ser	Ser	Ser
	88	Ala	Ala	Ala	Ala	Ala
	89	Val	Val	Thr	Thr	Val
	90	Tyr	Tyr	Tyr	Tyr	Tyr
	91	Phe	Phe	Tyr	Tyr	Tyr
	92	Cys	Cys	Cys	Cys	Cys
	93	Thr	Thr	Ala	Ala	Ala
	94	Lys	Lys	Arg	Arg	Arg
CDR3	95	Glu	Glu	Asp	Asp	Ser
	96	Glu	Glu	Arg	Gly	Gly
	97	Tyr	Tyr	Gly	Phe	Tyr
	98	Asp	Asp	Gly	Leu	Tyr
	99	Tyr	Tyr	Arg	Arg	Gly
	100	Asp	Asp	Asp	Asp	Ser
	100A	Thr	Thr	---	---	Phe
	100B	---	---	---	---	Val
	100C	---	---	---	---	Gly
	100D	---	---	---	---	---
	100E	---	---	---	---	---
	100F	---	---	---	---	---
	100G	---	---	---	---	---
	100H	---	---	---	---	---
	100I	---	---	Trp	Trp	---
	100J	---	---	Tyr	Tyr	---
	100K	Leu	Leu	Phe	Phe	Phe
	101	Asp	Asp	Asp	Asp	Ala
	102	Tyr	Tyr	Val	Val	Tyr
FR4	103	Trp	Trp	Trp	Trp	Trp
	104	Gly	Gly	Gly	Gly	Gly
	105	Gln	Gln	Ala	Ala	Gln
	106	Gly	Gly	Gly	Gly	Gly
	107	Thr	Thr	Thr	Thr	Thr
	108	Ser	Ser	Thr	Thr	Leu
	109	Val	Val	Val	Val	Val
	110	Thr	Thr	Thr	Thr	Thr
	111	Val	Val	Val	Val	Val
	112	Ser	Ser	Ser	Ser	Ser
	113	Ser	Ser	Ser	Ser	Ala

FIG. 5

		3	17	20	27	33
FR1	1	Asp	Asp	Asp	Asp	Asp
	2	Ile	Ile	Ile	Ile	Ile
	3	Val	Val	Val	Val	Val
	4	Leu	Leu	Leu	Met	Met
	5	Thr	Thr	Thr	Thr	Thr
	6	Gln	Gln	Gln	Gln	Gln
	7	Ser	Ser	Ser	Ser	Ser
	8	Pro	Pro	Pro	His	His
	9	Ala	Ala	Ala	Lys	Lys
	10	Ser	Ser	Ser	Phe	Phe
	11	Leu	Leu	Leu	Met	Met
	12	Ala	Ala	Ala	Ser	Ser
	13	Val	Val	Val	Thr	Thr
	14	Ser	Ser	Ser	Ser	Ser
	15	Pro	Leu	Leu	Val	Val
	16	Leu	Gly	Gly	Gly	Gly
	17	Gly	Gln	Gln	Asp	Asp
	18	Gln	Arg	Arg	Arg	Arg
	19	Arg	Ala	Ala	Val	Val
	20	Ala	Ser	Thr	Ser	Thr
	21	Thr	Ile	Ile	Ile	Ile
	22	Ile	Ser	Ser	Thr	Thr
	23	Ser	---	---	Cys	Cys
CDR1	24	Tyr	Tyr	Tyr	Lys	Lys
	25	Arg	Arg	Arg	Ala	Ala
	26	Ala	Ala	Ala	Ser	Ser
	27	Ser	Ser	Ser	Gln	Gln
	27A	Lys	Lys	Lys	---	---
	27B	Ser	Ser	Ser	---	---
	27C	Val	Val	Val	---	---
	27D	Gln	Ser	Ser	---	---
	27E	Leu	Thr	Thr	---	---
	27F	His	---	---	---	---
	28	Leu	Ser	Ser	Asp	Asp
	29	Ala	Gly	Gly	Val	Val
	30	Ile	Tyr	Tyr	Asn	Thr
	31	Val	Ser	Ser	Thr	Thr
	32	Tyr	Tyr	Tyr	Ala	Asp
	33	Met	Met	Met	Val	Val
	34	His	His	His	Ala	Ala
FR2	35	Trp	Trp	Trp	Trp	Trp
	36	Asn	Asn	Asn	Tyr	Tyr
	37	Gln	Gln	Gln	Gln	Gln
	38	Gln	Gln	Gln	Gln	Gln
	39	Lys	Lys	Arg	Lys	Lys
	40	Pro	Pro	Pro	Pro	Pro
	41	Gly	Gly	Gly	Gly	Arg
	42	Gln	Gln	Gln	Gln	Gln
	43	Pro	Pro	Pro	Ser	Ser
	44	Pro	Pro	Pro	Pro	Pro
	45	Arg	Arg	Arg	Lys	Lys
	46	Leu	Leu	Leu	Leu	Leu
	47	Leu	Leu	Leu	Leu	Leu
	48	Ile	Ile	Ile	Leu	Ile
	49	Tyr	Tyr	Tyr	Tyr	Tyr
CDR2	50	Leu	Leu	Leu	Ser	Ser
	51	Val	Val	Val	Ala	Ala
	52	Ser	Ser	Ser	Ser	Ser
	53	Asn	Asn	Asn	Tyr	Tyr
	54	Leu	Leu	Leu	Arg	Arg
	55	Glu	Glu	Asp	Tyr	Tyr
	56	Ser	Ser	Ser	Thr	Thr
	57	Gly	Gly	Gly	Gly	Gly
	58	Val	Val	Val	Val	Val
	59	Pro	Pro	Pro	Pro	Pro
	60	Ala	Ala	Ala	Asp	Asp
	61	Arg	Arg	Arg	His	Arg
	62	Phe	Phe	Phe	Phe	Phe
	63	Ser	Ser	Ser	Thr	Thr
	64	Gly	Gly	Gly	Gly	Gly
	65	Ser	Ser	Ser	Ser	Ser
	66	Gly	Gly	Gly	Gly	Gly
	67	Gly	Ser	Ser	Ser	Ser
	68	Gly	Gly	Gly	Gly	Gly
	69	Thr	Thr	Thr	Thr	Thr
	70	Asp	Asp	Asp	Asp	Asp
	71	Phe	Phe	Phe	Phe	Phe
	72	Thr	Thr	Thr	Thr	Thr
	73	Leu	Leu	Leu	Phe	Phe
	74	Asn	Asn	Asn	Thr	Thr
	75	Ile	Ile	Ile	Ile	Ile
	76	His	His	His	Ser	Ser
	77	Pro	Pro	Pro	Ser	Ser
FR3	78	Val	Val	Val	Val	Val
	79	Glu	Glu	Glu	Gln	Gln
	80	Glu	Glu	Glu	Ala	Ala
	81	Glu	Glu	Glu	Glu	Glu
	82	Asp	Asp	Asp	Asp	Asp
	83	Ala	Ala	Ala	Leu	Leu
	84	Ala	Ala	Ala	Ala	Ala
	85	Thr	Thr	Thr	Val	Val
	86	Tyr	Tyr	Tyr	Tyr	Tyr
	87	Tyr	Tyr	Tyr	Tyr	Tyr
	88	Cys	Cys	Cys	Cys	Cys
CDR3	89	Gln	Gln	Gln	Gln	Gln
	90	His	His	His	Gln	Gln
	91	Ile	Ile	Ile	His	His
	92	Arg	Arg	Glu	Tyr	Tyr
	93	Val	Gly	Gly	Ser	Ser
	94	Ala	Ala	Ala	Pro	Thr
	95	---	---	---	Pro	Ala
	95A	---	---	---	---	---
	95B	---	---	---	---	---
	95C	---	---	---	---	---
	95D	---	---	---	---	---
	95E	---	---	---	---	---
	95F	---	---	---	---	---
	96	Tyr	Tyr	Tyr	Leu	Trp
	97	Thr	Thr	Thr	Thr	Thr
FR4	98	Phe	Phe	Phe	Phe	Phe
	99	Gly	Gly	Gly	Gly	Gly
	100	Gly	Gly	Gly	Ala	Gly
	101	Gly	Gly	Gly	Gly	Gly
	102	Thr	Thr	Thr	Thr	Thr
	103	Lys	Lys	Lys	Lys	Lys
	104	Leu	Leu	Leu	Leu	Leu
	105	Glu	Glu	Glu	Glu	Glu
	106	Ile	Ile	Ile	Leu	Ile
	106A	---	---	---	---	---
	107	Lys	Lys	Lys	Lys	Lys

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EUROPEAN SEARCH REPORT

Application Number
EP 94 11 5683

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
A	US-A-5 208 146 (R. ERIE) * the whole document * ---	1-27	C12N15/13 C07K16/42
A	WO-A-89 00050 (AKZO NV) * claims * * examples * ---	1-27	
A	WO-A-93 10221 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) * the whole document * ---	1-27	
A	EUROPEAN JOURNAL OF CANCER AND CLINICAL ONCOLOGY, vol.24, no.5, May 1988, OXFORD, GB pages 829 - 838 Y. AOTSUKA ET AL. 'Identification of a malignant cell associated antigen recognized by a human monoclonal antibody.' * abstract * ---	1-27	
A	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE USA, vol.80, no.20, October 1983, WASHINGTON DC, USA pages 6327 - 6331 M. GLASSY ET AL. 'UC 729-6, a human lymphoblastoid B-cell line useful for generating antibody-secreting human-human hybridomas.' * abstract * --- -/--	1-27	

TECHNICAL FIELDS SEARCHED (Int.Cl.6)
C12N
C07K

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	16 March 1995	Nooij, F

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A	CANCER RESEARCH, vol.52, no.9, 1 May 1992, PHILADELPHIA PA, USA pages 2603 - 2609 W. TADDEI-PETERS ET AL. 'Quantitation of human tumor-reactive monoclonal antibody 16.88 in the circulation and localization of 16.88 in colorectal metastatic tumor tissue using murine antiidiotypic antibodies.' * abstract * ---	1-27	
P,A	MOLECULAR IMMUNOLOGY, vol.30, no.16, November 1993, OXFORD, GB pages 1481 - 1489 K. YAGO ET AL. 'Immunoglobulin variable region sequences of two human monoclonal antibodies directed to an onco-developmental carbohydrate antigen, lactotetraosylceramide (LcOse4Cer).' * abstract * -----	1-27	
			TECHNICAL FIELDS SEARCHED (Int.Cl.6)

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